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DISEASES

of the

CHEST

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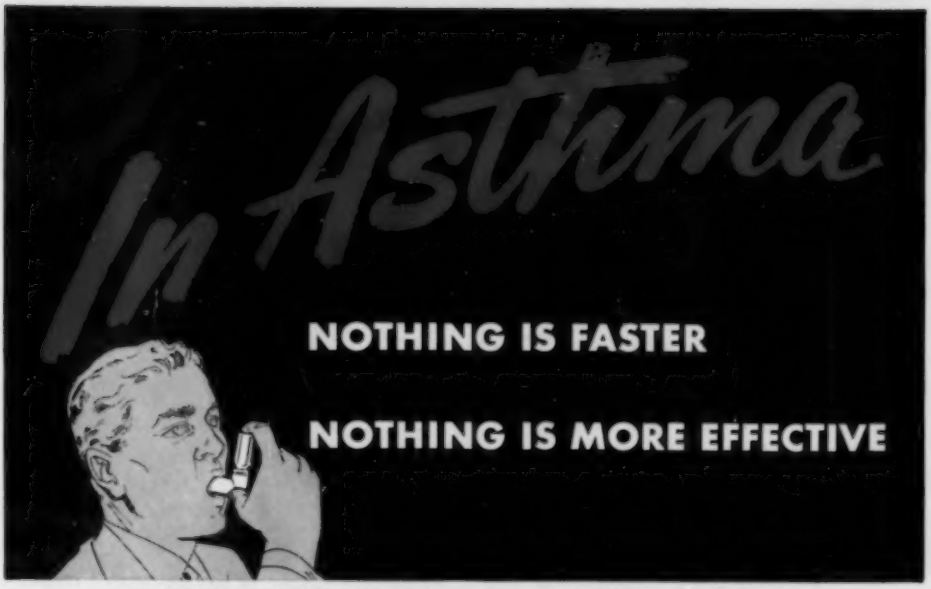

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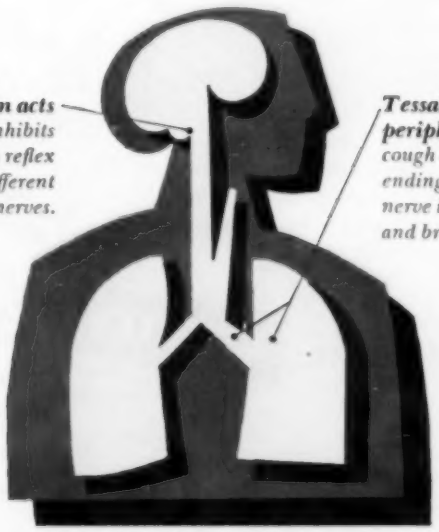
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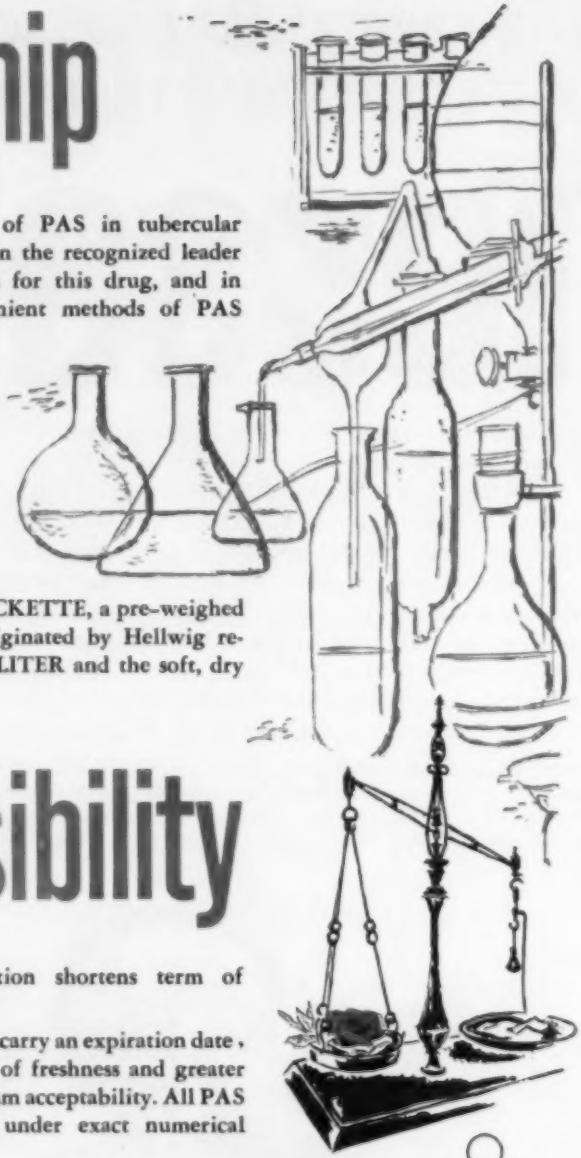

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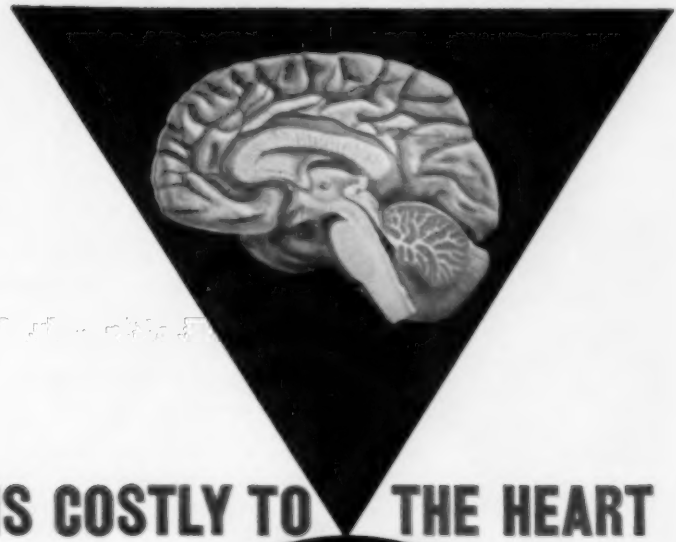

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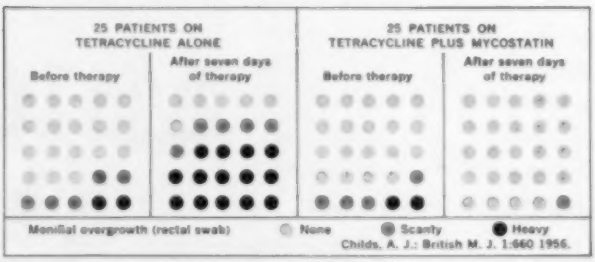

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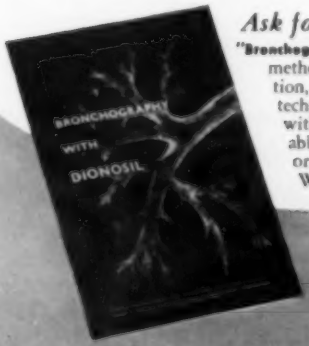

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[1]Dr. Samuel Phillips: *Calcium Benzoyl PAS*, Paper presented at 15th VA-Army-Navy Conference on Chemotherapy of Tuberculosis, St. Louis, Missouri, February 6-9, 1956.

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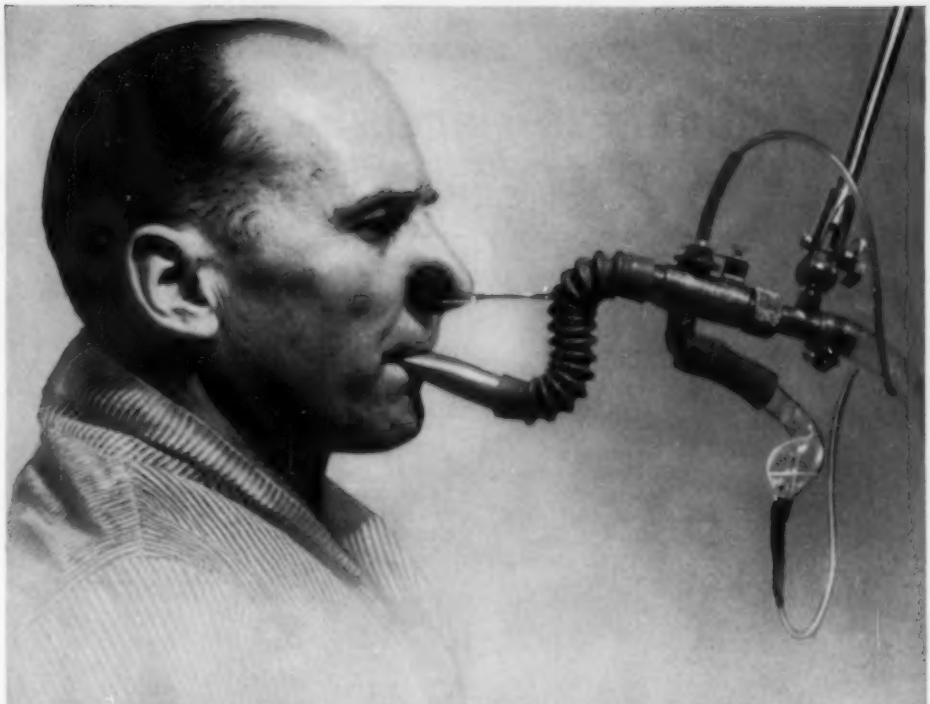

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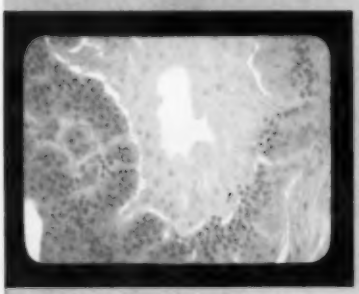

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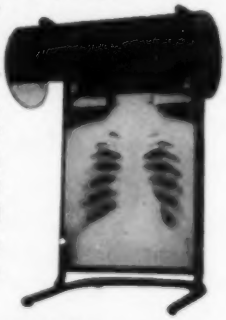

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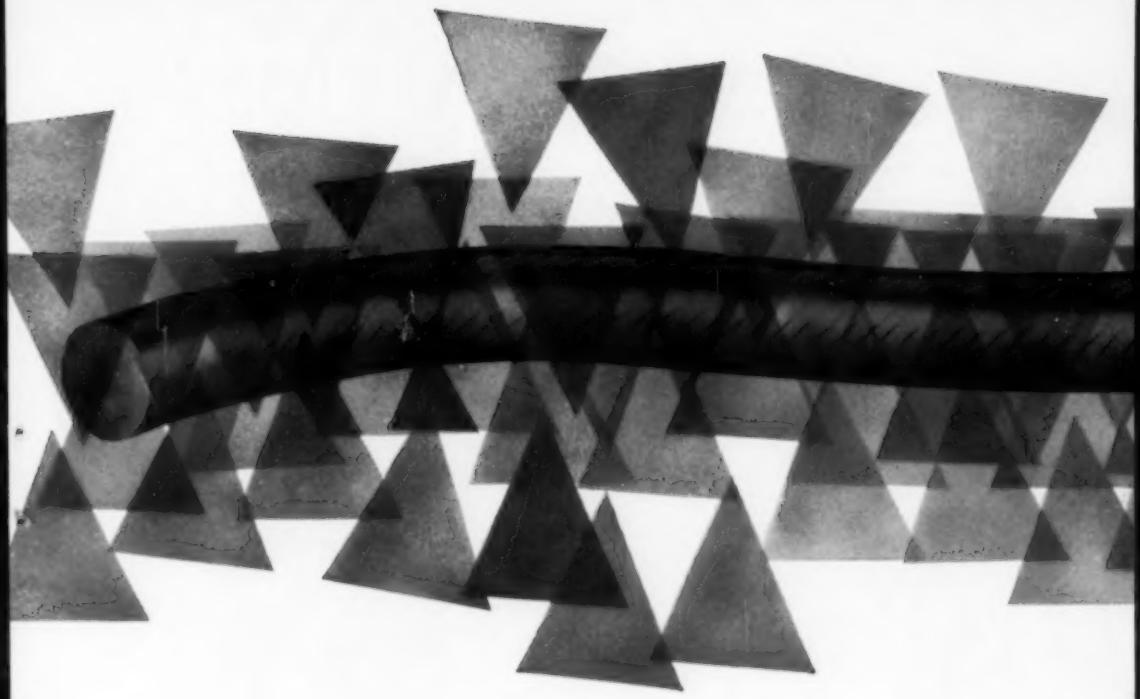

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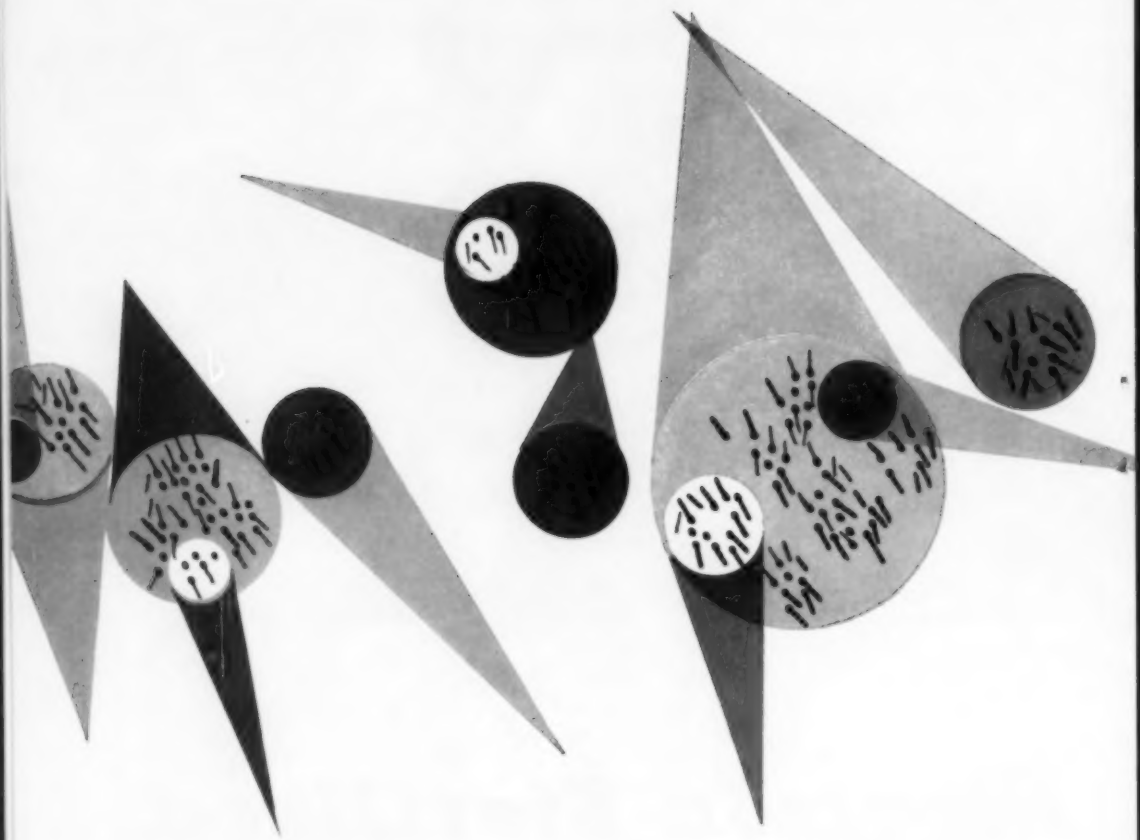

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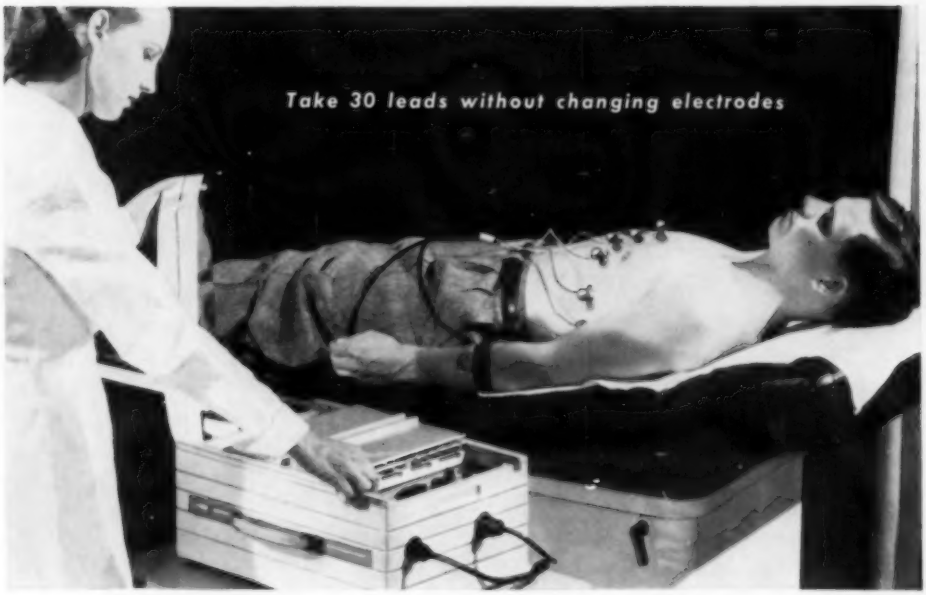

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Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.

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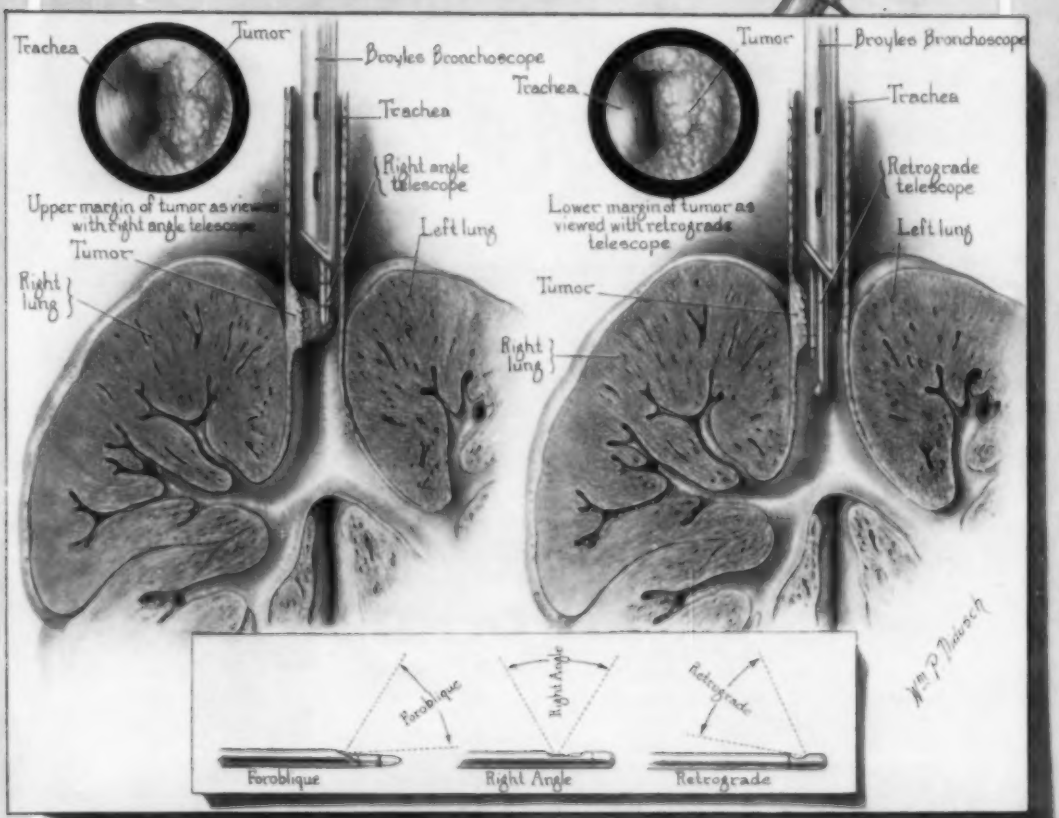

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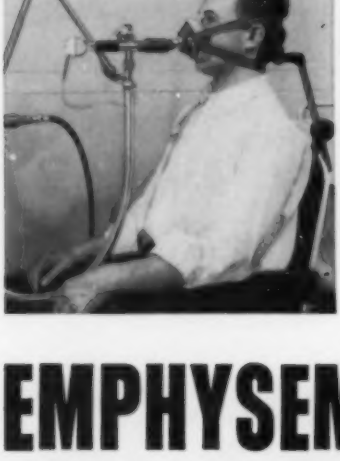

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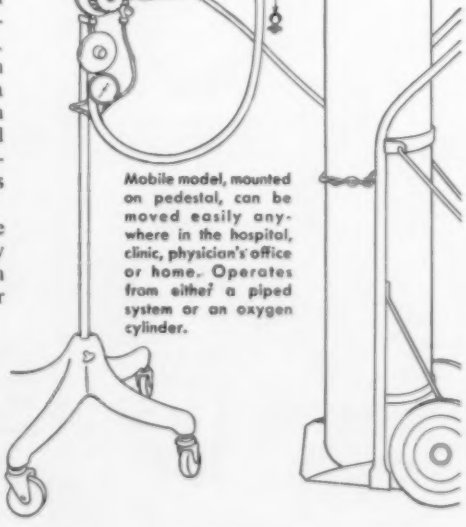

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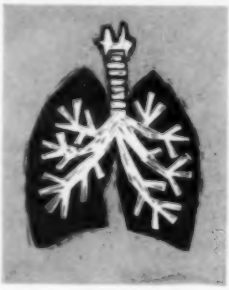

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1. Reports to the Squibb Institute of Medical Research, 1957. 2. Sherwood, H., and Cooke, R. A.: J. Allergy 28:97, 1957. 3. Hellman, L., et al.: American Rheumatism Association. Interim session, Nov. 23, 1956. 4. Berntsen, C. A., Jr., et al.: New York Rheumatism Association. Annual meeting, April 9, 1957, New York. 5. Freyberg, R. H., et al.: International Congress on Rheumatic Diseases, June, 1957, Toronto.

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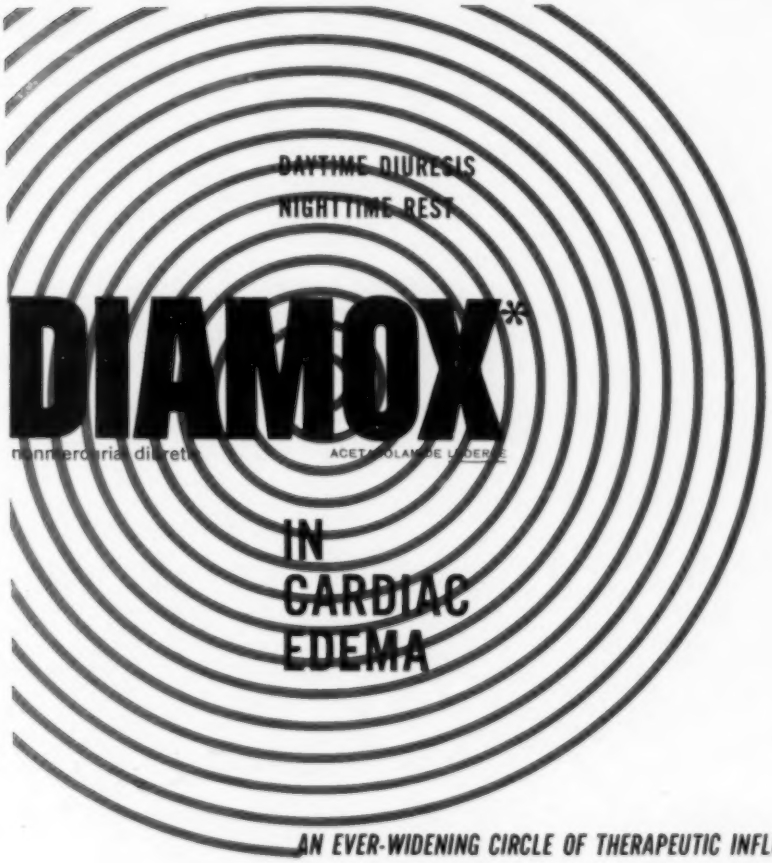

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1 Braveman, W. S.; Dexter, R. S., and Rubin, A. L.: Diamox (Acetazolamide) as an Oral Diuretic in Ambulatory Cardiac Patients. Am. Heart J. 54:284-290, 1957.

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California Chapter, Los Angeles, April 26
Georgia Chapter, Macon, April 29
Illinois Chapter, Chicago, April 15; Rockford, April 24
Louisiana Chapter, Baton Rouge, April 12
Missouri Chapter, St. Louis, April 13
New England States Chapter, Worcester, Mass., April 14
Ohio Chapter, Cincinnati, April 16
Oklahoma Chapter, Waggoner, April 19
Pennsylvania Chapter, Reading, April 16
Tennessee Chapter, Chattanooga, April 21
Texas Chapter, Houston, April 20

MAY

Arizona Chapter, Chandler, May 1
Florida Chapter, Miami Beach, May 11
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DISEASES of the CHEST

VOLUME XXXIII APRIL, 1958 NUMBER 4

An Aerosol Method of Producing Bronchial Secretions in Human Subjects: A Clinical Technic for the Detection of Lung Cancer

HYLAN A. BICKERMAN, M.D., F.C.C.P., EDITH E. SPROUL, M.D. and ALVAN L. BARACH, M.D., F.C.C.P.

New York, New York

The increasing importance of lung cancer as a major health problem has recently been emphasized by Gerhardt, Handy and Ferber[1] who compared the age-standardized incidence rates for cancer for the years 1942 and 1955 in New York State. In man, the outstanding change in incidence rates over the 14 year period was the 202 per cent increase in carcinoma of the lung and bronchus. Even more striking is the increase of 520 per cent in the death rate due to lung cancer among the male population over the past 22 years. In women, this increase was 75 per cent. Similar trends have been reported for other states and for the United States as a whole.[2]

The rising incidence of bronchogenic carcinoma makes early diagnosis a factor of vital importance. The number of patients diagnosed with lung cancer in an operable stage and with a reasonably good prognosis is still small. Lutwyche[3] in a review of 116 cases of bronchial carcinoma noted a considerable delay in diagnosis in one third of his series. At present, there is no unanimity of opinion regarding the value of chest roentgenograms in screening for early lung cancer. Opinions vary from the belief that most cases have already metastasized by the time they are suspected radiologically, to the conviction that many are still localized and resectable.[4]

Since the first report by Hampeln[5] in 1918 on the presence of malignant cells in the sputum of patients with bronchogenic carcinoma, a number of investigators[6-8] have confirmed the importance of cytologic examination in the diagnosis of lung cancer particularly in the early stages. Employing technics developed by Papanicolaou,[9] the accuracy of diagnosis by sputum cytology has ranged from 84 to 93.5 per cent in the various series published. Farber and his associates[10] reported a 90 per

From the Columbia University Research Service, Goldwater Memorial Hospital, the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian and Francis Delafield Hospitals.

This study has been supported by the American Cancer Society.

Presented at the 23rd Annual Meeting, American College of Chest Physicians, New York City, May 29-June 2, 1957.

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cent accuracy in the positive diagnosis of lung cancer when five or more sputum specimens were examined. This degree of accuracy declined sharply when fewer specimens were studied.

In formulating a screening program for the early detection of lung cancer in apparently healthy individuals, cytologic methods have been considered impractical since the vast majority of these subjects are asymptomatic and raise no sputum. An approach to this problem has been made by utilizing the principles and technic of producing sputum in human subjects by the inhalation of hypertonic saline aerosols. The preliminary results of such cytologic screening are reported in this paper.

Theoretical Considerations

The problem of depositing an aerosol on the tracheo-bronchial mucosa which would induce bronchial secretions in apparently healthy individuals and yield sputum specimens suitable for cytologic study raised certain considerations. Among the factors which determine the degree of retention of an aerosol and the sites of deposition within the respiratory tract are: particle size and density, vapor pressure, temperature and hygroscopic properties of the aerosol, and the rate and depth of respiration. Findeisin[11] showed that 97 per cent of solid particles of 1 micron radius and above are deposited within the lung. Particles of 3 micra in radius are taken out completely by the trachea, bronchi and bronchioles. The retention of aerosol droplets in the human respiratory tract as a function of particle radius and respiratory rate was studied by Wilson and La Mer.[12] A maximal retention of approximately 50 per cent occurred in the alveoli and bronchioles with particles of 1.0 micron in radius. The stability of a water droplet 0.5 micron in radius under ordinary conditions of humidity is only a fraction of a second due to its high evaporation rate. Furthermore, rapid absorption of isotonic aerosols took place within the tracheobronchial tree. Studies by Abramson[13] indicate that droplet evaporation is decreased with aerosols in a glycerin solution because of the reduction in vapor pressure, serving to stabilize the aerosol mist.

TABLE I
AGE AND SEX DISTRIBUTION OF 336 PATIENTS RECEIVING HYPERTONIC SALINE AEROSOLS

Groups*	Sex	Number of Subjects	Age Mean (Years)	Age Range
A	Male	125	55.3	21-90
	Female	78	53.1	18-86
B	Male	75	59.3	35-78
	Female	35	44.3	20-73
C	Male	20	58.9	30-75
	Female	3	51.0	50-52

*A—No evidence of pulmonary pathology
B—Chronic non-tuberculous pulmonary disease
C—Known or suspected malignancy

Using aerosols containing radioactive solium, Talbot, Quimby and Barach[14] found that the addition of 10 per cent propylene glycol to the aerosol solution results in a greater deposition within the lung than is produced by isotonic mists. Barach, Garthwaite and Bickerman[15] noted that the comfort of inhaling penicillin aerosols is enhanced by providing a warm aerosol, and in addition, higher blood levels are obtained as compared with cold aerosols indicating an increased deposition of the penicillin mist.

The osmotic effect of hypertonic saline solutions for the purpose of this project was suggested by a study of Barach, Mason and Jones[16] who noted a marked and instantaneous increase in plasma volume following the intravenous administration of 100 ml. of 15 per cent saline solution. It seemed likely that the impingement of an adequate number of hypertonic saline droplets upon the bronchial mucosa would, osmotically, induce transudation. Such a bronchial transudate might then wash exfoliating cells from the regions of aerosol deposition into the material subsequently expectorated.

Methods

With the above considerations in mind, various concentrations of saline solution ranging from 3 to 15 per cent were employed to induce sputum production. A 10 per cent sodium chloride solution has been used in the majority of instances since the incidence of irritation appeared to be less than with the 15 per cent concentration. It was necessary to limit the saline aerosol to 3 per cent in some patients with bronchial asthma and pulmonary emphysema since the more hypertonic solutions appeared to accentuate obstructive dyspnea. Initially, 40 per cent propylene glycol

FIGURE 1: Photograph illustrating the inhalation of warm hypertonic saline aerosol generated in a high flow nebulizer by means of an air pump.

was employed but this hygroscopic aerosol was too viscid and often occluded the nebulizer. The addition of 15 or 20 per cent propylene glycol to the saline solution provided a stable mist which did not usually interfere with continuous nebulization.

Since nebulization of a large quantity of aerosol solution within a limited period of 10 to 20 minutes appeared desirable, high-flow nebulizers which produced a relatively large particle size ranging between 1 to 10 micra in radius were employed. A small pump producing an air-flow of 5 to 7 liters per minute through the nebulizer generated the aerosol mist. Since initial studies had clearly shown that irritation was reduced and the comfort of inhalation enhanced by warming the aerosol, the solution within the nebulizer was heated by placing the reservoir of the nebulizer over a steam generator or electric coffee percolator.* The nebulizers originally employed included a large capacity baffle-less Vaponefrin nebulizer** and the Aero-Mist nebulizer.† More recently, a high-flow nebulizer‡ has been developed which nebulizes 1 ml. of hypertonic saline per minute, and incorporates a thermostatically controlled heating unit adjusted so as to provide an aerosol warmed to 105° to 130° C. A photograph and line drawing of this nebulizer are illustrated in Figures 1 and 2.

Procedure

A total of 336 patients from the wards of the Goldwater Memorial Hospital, Francis Delafield Hospital and the Asthma Clinic of the Co-

TABLE II
THE RECOVERY OF SPUTUM IN 336 SUBJECTS FOLLOWING THE INHALATION OF HYPERTONIC (10 AND 15 PER CENT) SALINE AEROSOLS

Group*	Number of Subjects	Results		
		Positive**		Negative
		Number	Per Cent	Number
A-I	180	155	86.1	25
II	23	0	0	23
B	110	99	90.0	11
C	23	23	100.0	0
TOTAL	336	277	82.5	59
Corr. Total (excl. A-II)	313	277	88.5	36

*A—No pulmonary pathology (A-II pts. with impaired cough reflex)
B—Chronic non-tuberculous pulmonary disease
C—Suspected malignancy

**mucoid sputum exceeding 1 ml.

*West-Bend Aluminum Co., West Bend, Wisconsin.

**Manufactured by Vaponefrin Co., Upper Darby, Pennsylvania.

†Obtained from Medical Specialties, Inc., Boonton, New Jersey.

‡Manufactured by O. E. M. Corp., East Norwalk, Connecticut. Homemakers' Products Corp. manufactures an inexpensive, effective apparatus providing the higher temperatures now generally employed.

lumbia-Presbyterian Medical Center participated in the study. They were divided into three groups:

Group A: This group consisted of 203 patients with a wide variety of illnesses but with no evidence of pulmonary disease by clinical and roentgenologic study. These individuals were classified as apparently healthy with respect to the respiratory system and had no cough or spontaneous sputum.

Group B: This group consisted of 110 patients with chronic non-tuberculous pulmonary disease in whom the diagnosis of bronchial asthma, pulmonary emphysema and chronic bronchitis predominated.

Group C: This group consisted of 23 patients with known or suspected malignancy involving the lung or other organs. These patients were selected in such a manner that neither the technician who performed the test nor the pathologist who examined the sputum were aware of the diagnosis. Certain statistics for each of the three groups are shown in Table I.

Each subject inhaled the warmed aerosol produced by the continuous nebulization of a solution containing 10 or 15 per cent sodium chloride and 20 per cent propylene glycol for periods of 10 to 20 minutes. Because of an increased incidence in wheezing and coughing among the patients in Group B with bronchopulmonary pathology, the salt content of the aerosol was subsequently lowered to 3 per cent, as mentioned above, and was often preceded by an inhalation of 0.2 ml. of 2.25 per cent racemic

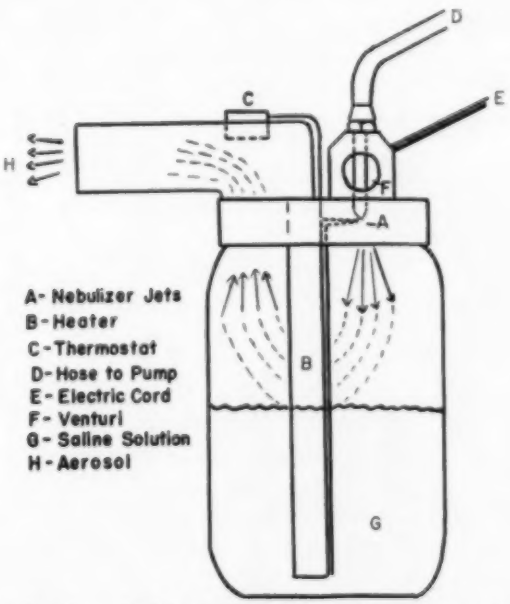

FIGURE 2: Line drawing of high-flow nebulizers with a thermostatically controlled heating element. Aerosol particle size ranges between 1 to 10μ in radius.

epinephrine (Vaponefrin)* or 0.4 per cent isuprel.** The latter procedure was followed in the last 20 patients of this group. All of the material expectorated during, and for 10 minutes following the aerosol inhalation was collected and measured. Gross appearance with respect to color, consistency and the presence of mucoid or muco-purulent shreds or plugs were noted. The recovery of mucoid material exceeding 1 ml. in amount indicated, in our opinion, that the specimen had been obtained from the tracheo-bronchial passageway since it could readily be distinguished from saliva, especially after the expectorated material was added to an equal volume of 70 per cent ethyl alcohol.

Spontaneous sputum collections were performed on 16 patients with chronic bronchitis prior to aerosol therapy. Each subject was then given an inhalation of 10 per cent sodium chloride and 20 per cent propylene glycol. Specimens obtained prior to the aerosol and after the inhalation of the hypertonic saline solution were analyzed quantitatively for total chloride content.

Sputum specimens following aerosol therapy were collected from 74 subjects including 19 patients with suspected malignancy, placed in an equal volume of 70 per cent ethyl alcohol and processed for cytologic study.

Results

Following the inhalation of hypertonic saline aerosols, specimens of sputa were obtained from 277 of the 336 patients treated. This is illustrated in Table II. Initially it was observed that 76.4 per cent of the patients in Group A yielded sputum specimens whereas 90 per cent of the patients with pulmonary disease and 100 per cent of the group with suspected malignancy raised adequate sputum samples. On further examination of the negative responders in Group A, it was found that 23 of these

TABLE III

DURATION OF INHALATION AND AMOUNT OF AEROSOL ADMINISTERED TO 277 SUBJECTS WITH RECOVERABLE SPUTUM

Groups*	No. of Subjects	Per Cent Concentration Saline Aerosol	Means Aerosol Admin.		Sputum Collected (Ml.)
			Amount (Ml.)	Time (Ml.)	
A	155	10 or 15	7.7	15.0	5.7
B-I	79	10	9.2	12.0	8.0
II	20	3	8.8	11.7	8.0
C	23	10	10.3	13.0	7.2

*A—No pulmonary pathology
B—Chronic non-tuberculous pulmonary disease
(B-II—asthmatics receiving 3 per cent saline)
C—Suspected malignancy

*Vaponefrin Co., Upper Darby, Pa.

**Isoproterenol, 0.4 per cent, was mixed with phenylephrine 2.0 per cent, supplied as a Nebu-Isophrin by Homemakers' Products Corporation, Englewood Cliffs, New Jersey.

patients had neurologic disorders with marked impairment of the cough mechanism. These included 16 patients with hemiplegia, three with poliomyelitis, two with muscular dystrophy and two with meningovascular syphilis. Correcting the data by excluding these individuals, (Group A-II), resulted in an 86.1 per cent recovery of sputum from patients in Group A and an 88.5 per cent recovery for the combined series.

The amount of aerosol administered and the duration of each treatment were roughly comparable in all three groups. This is illustrated in Table III. Minor variations were related to the different nebulizers and aerosol pumps employed in the early phases of the study. Although the amount of sputum recovered varied widely from subject to subject, in general, those in Groups B and C gave higher yields than the subjects with no apparent pulmonary pathology. It must be recognized that the amount of sputum collected was at best a rough estimate since admixture with saliva and aerosol made quantitative measurement impossible. Nevertheless a sufficient amount of material was available in almost every instance for cytologic study.

Preliminary studies with cold hypertonic saline areosols resulted in frequent complaints of a sense of irritation to the upper respiratory tract as manifested by scratchiness of the throat, hoarseness and cough. This was materially reduced when the aerosols were warmed to 40 to 44° C.

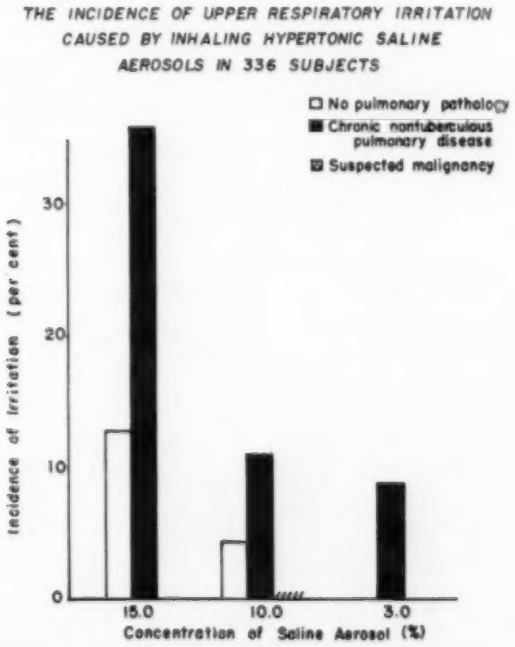

FIGURE 3: The incidence of upper respiratory irritation caused by inhaling hypertonic saline aerosols in 336 subjects, illustrating a positive correlation between the concentration of saline and per cent increase in irritation.

The incidence of upper respiratory irritation for the warmed aerosols is illustrated in Figure 3. Only 10 per cent saline solutions were employed in the patients with suspected malignacy and none of these reported any irritative symptoms. It is evident that a positive correlation exists between the incidence of irritation and the degree of hypertonicity of the saline aerosol. As might be expected, the per cent of subjects experiencing irritation was higher for those in Group B with asthma and pulmonary emphysema than for the subjects in Group A when either 10 or 15 per cent saline was inhaled. With a warmed 10 per cent saline aerosol, only three (4.3 per cent) in Group A, with no evidence of pulmonary pathology, complained of irritation.

A comparison of the total chloride content of the sputum collected on 16 subjects in Group B before and after administering an average of 8 ml. of 10 per cent saline aerosol showed a slight but insignificant increase in the chloride content of the sputum following the inhalation of the hypertonic saline solution. This is illustrated in Table IV. These findings would appear to indicate an osmotic effect resulting in the rapid dilution of the hypertonic aerosol droplets by bronchial transudate.

Cytologic Studies

Sputum specimens obtained from 74 subjects following inhalations of 10 per cent saline aerosol were subjected to cytologic study. Since material was recovered from patients with a variety of pulmonary disorders as well as from individuals free of lung disease, the character of the specimens varied greatly. In general, the induced sputum of "normal" individuals contained little gross particulate matter and appeared pale, whereas specimens from patients with pulmonary pathology appeared more mucoid and in some instances contained fresh muco-purulent plugs.

1. Method of Processing Specimen: The specimens arrived in the laboratory in glass bottles containing equal volumes of 70 per cent alcohol which had been added to the material expectorated. The entire contents were centrifuged for 15 minutes at 1500 rpm and the supernatant fluid decanted. The superficial part of the sediment was transferred to glass slides with a small spatula and two to four smears were prepared. Routine preparation included one hematoxylin-eosin and one mucicarmine

TABLE IV

COMPARISON OF THE CHLORIDE CONTENT OF THE SPUTUM COLLECTED FROM 16 PATIENTS BEFORE AND AFTER INHALING 10 PER CENT SALINE AEROSOL

	Number of Subjects	Mean Amount Sputum (ml.)	Mean Chloride Content	
			Mgs. Per Cent	S. D.
Before Aerosol	16	3.8	197.0	72.0
—mean of 8.3 ml. 10 per cent saline aerosol administered—				
After Aerosol	16	6.4	244.7	80.8

stain. The remainder of the sediment was fixed in Bouin's solution, embedded in paraffin in the autotechnicon and sectioned. At least one hematoxylin-eosin and one mucicarmine stained slide were routinely prepared.

II. Cytologic Observations: a) Preservation of cells: No distortion of cells which might be attributed to hypertonic saline were observed. There was no shrinkage or crenation. The nucleus and cytoplasm seem to be preserved in relative proportion. Nuclear chromatin pattern was distinct and the granular or vacuolar character of the cytoplasm was maintained. The cells did not appear altered as compared with their spontaneously ejected counterparts. Variation in cell preservation and staining qualities could be attributed to the vicissitudes of the autotechnicon and technician.

b) Cell types: Sixteen of the 74 specimens contained only superficial squamous cells and leukocytes. These were regarded as unsatisfactory for study since there was no evidence that any of the material came from the lower respiratory tract. Most sediments contained alveolar phagocytes with anthracotic pigment and rarely some hemosiderin or fat vacuoles. The phagocytes varied in numbers about as one would expect from different individuals. Even healthy subjects yielded phagocytes (all were city dwellers or workers) and often in considerable quantities. The presence of these cells was regarded as an index of the depth from which the specimen was obtained since they occurred in clumps, which would be an unlikely finding if they were in the trachea or pharynx.

Bronchial epithelial cells were less numerous than alveolar phagocytes

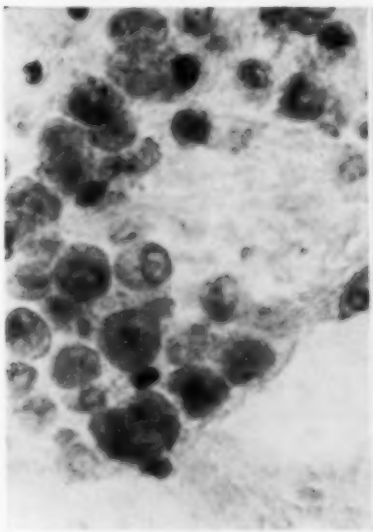

FIGURE 4

FIGURE 5

Figure 4: Photomicrograph of the sputum smear of a subject with hypertension (Group A) illustrating clusters of columnar, ciliated bronchial epithelial cells of normal character.—*Figure 5:* Smear of the sputum obtained from a patient with severe bronchial asthma (Group B) showing bronchial epithelium distended with mucus. One slender cell presents a ciliated border. This amount of mucus is abnormal.

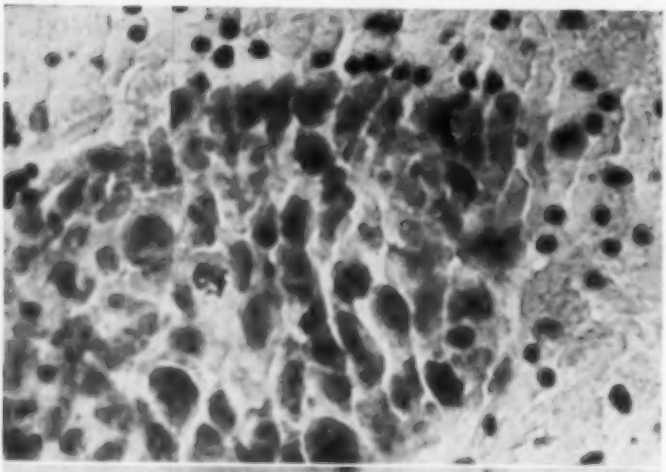

FIGURE 6

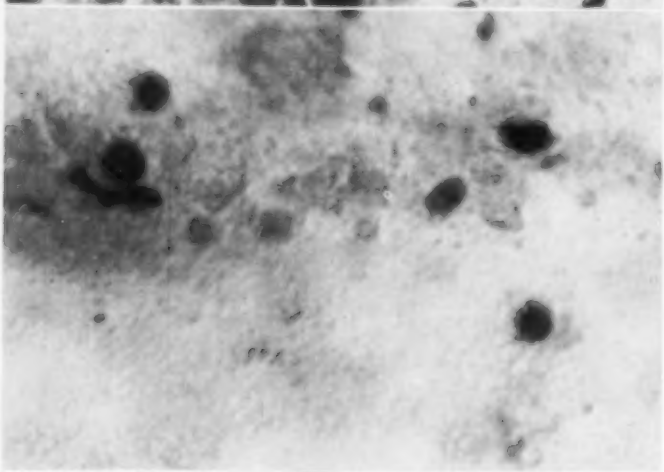

FIGURE 7

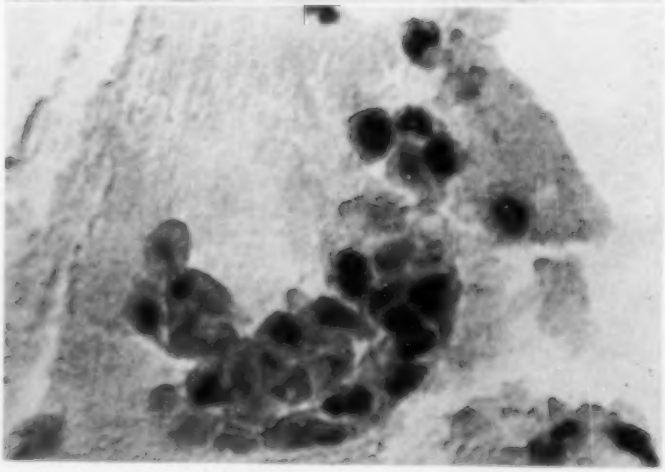

FIGURE 8

but were very well preserved. In general these cells showed less alteration than that observed in spontaneous sputum. Cilia were easily seen. This is illustrated in Figure 4. One to three nuclei with fine chromatin appeared at the apposing end of the cell and the cytoplasm was finely granular or vacuolated. The vacuoles sometimes contained mucicarminophilic material. In the material from several patients bronchial epithelium distended with mucus was abundant. The photomicrograph (Figure 5) of a smear from sputum obtained from a patient with severe bronchial asthma reveals bronchial epithelium distended with mucus. Polymorphonuclear neutrophils and lymphocytes were readily identified. Occasionally eosinophils were abundant.

The abnormal cells were not numerous, occurring in six of the specimens. None were found in material from healthy individuals. The benign abnormalities took the form of strips of cuboidal cells resembling swollen alveolar lining cells such as one sees about the air spaces in a lung with thickening of the alveolar walls. There were also cuboidal squamous cells with relatively large nuclei resembling parabasal cells which may have represented squamous metaplasia in the bronchial tree. In this series, cancer appeared only as squamous carcinoma. The malignant cells occurred individually and in clumps. One patient produced pieces of cohesive tumor cells. Figures 6 and 7 show squamous carcinoma cells from the cell block and smear respectively on sputum recovered from a patient with known squamous cell carcinoma of the lung. A cluster of malignant cells is illustrated in Figure 8 recovered in the sputum of a patient with epidermoid carcinoma of the lung.

TABLE V
RESULTS OF CYTOLOGIC STUDIES PERFORMED ON SPUTUM RECOVERED FROM 74 SUBJECTS FOLLOWING INHALATION OF 10 PER CENT SALINE AEROSOL

		CYTOLOGIC EXAMINATION			
Group*	Number of Subjects	Positive for Malign. Cells	Abnorm. Cells Suspicious Mal.	Negative for Malign. Cells**	Unsatisfact. Specimen***
A	27			23	4
B	28			21	7
C	19	4	2	8	5
TOTAL	74	4	2	52	16

*A—No pulm. path. B—Chronic pulm. disease. C—Suspected malignancy
**Specimen contained well preserved respiratory epithelium
***insuff. quantity, no respir. epith., or purulent debris

See Figures on Opposite Page

Figure 6: A sheet of squamous carcinoma cells showing hyperchromatic nuclei, large nucleoli and mitotic figures recovered from the sputum of a patient with a known squamous cell carcinoma of the lung (Group C, cell block).—*Figure 7:* Individual malignant cells from the same patient with squamous cell carcinoma. The nuclei are relatively large, irregular and hyperchromatic with scanty cytoplasm (smear).—*Figure 8:* Cell block on the sputum recovered from a patient with epidermoid carcinoma of the left lung (Group C) showing a small cluster of malignant cells having relatively large, dark irregular nuclei and scanty cytoplasm. Several cells are degenerated.

A summary of the results of the cytologic study is shown in Table V. Fifty-eight (78.5 per cent) of the 74 specimens were judged to be representative samples of material from the lower respiratory tract satisfactory for diagnosis. Of these six from the group with suspected malignancy contained abnormal cells. Sixteen specimens were regarded as unsatisfactory for study since they contained only superficial squamous cells and leukocytes.

It was of interest to analyze the cytologic reports on the sputum obtained from the 19 patients in Group C which had been carried out in a "double-blind" fashion. This is illustrated in Table VI. Of the eight patients with documented primary or metastatic carcinoma of the lung, five of the sputum specimens induced by aerosol were positive for malignant cells. There were no false negatives in this group. Seven of the eight with malignancy in other organs not involving the lungs had no abnormal cells in their sputum, and one specimen was unsatisfactory for study. Of the sputum samples in the three patients with suspicious pulmonary infiltration on x-ray, one contained abnormal cells suggestive of squamous cell carcinoma, one was negative (subsequently diagnosed as tuberculosis) and one was unsatisfactory. Although conclusions cannot be drawn from this small series, the results of the cytologic study yielded no false positive or negative findings in those patients in whom a diagnosis had been established.

Discussion

Of the various factors which have been considered in an effective screening program for lung cancer, those of special importance include: 1) simplicity of technic, 2) non-injurious character of the procedure, 3) acceptance of the method by the subjects tested so that repeat studies are readily available, and 4) adequate criteria for establishing the diagnosis in order that the number of false positive and negative reports be minimal.

TABLE VI

ANALYSIS OF CYTOLOGIC STUDIES ON SPUTUM RECOVERED FROM 19 PATIENTS WITH KNOWN OR SUSPECTED MALIGNANCY (GROUP C) FOLLOWING INHALATION OF 10 PER CENT SALINE AEROSOL

Group C	Number of Subjects	Positive or Suspicious Mal.	Negative for Malign. Cells	Unsatisfact. Specimen*
1. Known Bronchogenic Carcinoma	7	4	0	3
2. Known Metast. Ca. to lung	1	1	0	0
3. Suspected lung cancer	3	1	1	1
4. Known or suspect. Ca. elsewhere	8	0	7	1
TOTAL	19	6	8	5

*purulent exudate predom., no respiratory epithelium seen.

The recovery of sputum adequate for cytologic study in 88.5 per cent of the combined series of 336 subjects following a single treatment with hypertonic aerosols justifies the extension of this program to a larger series. It is quite possible that negative responders might be induced to raise sputum following a second or third course of treatment with saline aerosol. Further study is required to ascertain whether conversion of these negative responders would occur with higher concentrations of saline aerosol. In addition, the effect of mechanical coughing by exsufflation with negative pressure following the inhalation of the saline aerosol may assist in raising bronchial secretions from the smaller bronchi and bronchioles particularly in those individuals with a weak or ineffective spontaneous cough.

The various alterations in cell morphology and the many bizarre forms of respiratory epithelium observed on cytologic study of sputum from patients with chronic pulmonary disease have recently been reported by Papanicolaou,[16] and Farber and his associates[17] who emphasized the need for rigid criteria in differentiating apparently benign metaplastic changes from carcinoma. From these reports and others, there is some evidence that the bronchial epithelium reaction leading to malignancy may be manifest for some time before the clinical diagnosis of lung cancer is possible.

Cytologic examination of the 74 sputum specimens recovered following the inhalation of 10 per cent saline aerosol indicated that the majority of the specimens expectorated contained respiratory epithelium and alveolar phagocytes. Cellular morphology was well preserved so that the clear cut differentiation between abnormal and normal cells was readily apparent to the experienced pathologist. In addition to the value of this method of obtaining sputum for the cytologic diagnosis of lung malignancy, the importance of bacteriologic as well as cytologic examination of induced sputum deserves further emphasis, especially in those patients with undiagnosed respiratory disease from whom no spontaneous sputum is available for study.*

SUMMARY

A method of obtaining sputum from the respiratory tract of "normal" individuals, patients with chronic non-tuberculous pulmonary disease, and patients with known or suspected malignancy is reported. The basis of this procedure involves the inhalation of warm, hygroscopic saline aerosols.

*Since this paper was written significant developments in the principles and technics of aerosol deposition have been made. At temperatures of 120° to 130° F., 10 liters of air contain 0.185 gm H_2O, at 120° F., 0.789, at 140° F. 1.302 gm H_2O. Over a period of 30 minutes inhalation approximately 11 cc. of water would theoretically be deposited on the laryngo-tracheo-bronchial mucous membrane at 120° F., and 39 cc. at 140° F. In an aerosol administered at 98° F. the particles are preserved by the humidified atmosphere but significant *enhanced* "rain-out" effect takes place *above* body temperature. The clinical advantages of inhaling aerosols with controlled temperatures of 120° F. and 130° F. in patients with bronchial asthma, pulmonary emphysema, and a variety of respiratory disorders characterized by difficulty in eliminating retained bronchial secretions will be reported later. (Barach, Alvan L., Beck, G. J., and Bickerman, H. A.).

Approximately 10 ml. of a 10 or 15 per cent saline aerosol containing 20 per cent propylene glycol was administered to a total of 336 subjects. Mucoid sputum specimens suitable for cytologic examination were recovered in 88.5 per cent of the entire series. Of special interest as a possible screening technic for the cytologic diagnosis of lung cancer was the production of sputum in 86 per cent of 180 subjects who had no evidence of pulmonary disease, and no cough or spontaneous sputum. Only three subjects in this group noted a slight irritation on inhaling the warm 10 per cent saline aerosol.

Cytologic studies of the sputum recovered from 74 subjects following the inhalation of 10 per cent saline showed that 79 per cent of the specimens were satisfactory for diagnosis. In five of the eight patients with documented primary or metastatic carcinoma in the lung, sputum preparations were positive for malignant cells. There were no false negative reports. Since all of the examinations were performed on single specimens, it is evident that cytologic study of repeated specimens obtained in a similar manner might increase the possibilities of accurate diagnosis. It is the opinion of our cytologist (E. E. S.) that this method of inducing sputum may be expected to demonstrate tumor cells from symptomless individuals before spontaneous sputum arises since the specimens obtained by hypertonic saline aerosol are entirely adequate for study.

Inhalation of nebulized 20 per cent propylene glycol at a temperature of 120° F. is employed to facilitate expectoration of retained secretions in patients with bronchopulmonary disease.

RESUMEN

Se describe un método para obtener esputo de las vías respiratorias de los individuos "normales" con enfermedad crónica no tuberculosa y enfermos sospechosos o averiguados de padecimientos malignos.

La base de este procedimiento radica en la inhalación de aerosoles calientes, de soluciones salinas higroscópicas.

Aproximadamente se usaron 10 ml. al 10 o 15 por ciento de un aerosol conteniendo 20 por ciento de propilen glicol en un total de 336 sujetos. Se obtuvo un espécimen mucoide adecuado para estudio citológico en 88.5 por ciento de los casos.

Es de interés especial este método como uno para la detección del cáncer por la citología ya que se obtuvo esputo en 86 por ciento de personas entre 180 sujetos que no tenían evidencia de enfermedad ni tos ni expectoración. Sólo tres personas de este grupo notaron ligera irritación al inhalar la solución caliente al diez por ciento en aerosol.

Los estudios citológicos en el esputo de 74 personas después de la inhalación de la solución salina al 10 por ciento, mostró que 79 por ciento de los especímenes fueron satisfactorios para el diagnóstico. En cinco de ocho enfermos comprobados de carcinoma primario o metastásico las preparaciones de esputos fueron positivas para células malignas. No hubo informes falsos negativos. Puesto que todos los exámenes se hicieron en sólo una muestra, es evidente los estudios en muestras repetidas hechas

en forma similar han de dar mayor proporción de diagnósticos exactos. El citologista opina (E.E.S.) que este método de provocar el esputo puede esperarse que muestre celdillas tumorales de individuos asintomáticos antes de que obtenga esputo espontáneo ya que los especímenes fueron completamente adecuados para el estudio.

RESUME

L'auteur présente une méthode qui permet d'obtenir des crachats provenant de l'arbre respiratoire chez des individus "normaux," chez des malades atteints d'affections pulmonaires chroniques non tuberculeuses, et chez des malades atteints d'affections malignes, connues ou soupçonnées. La base de ce procédé comprend l'inhalation d'aérosols salins, chauds et hygroscopiques.

Environ 10 cc. d'un aérosol à 10 ou 15% de sel, contenant 20% de glycol propylene, a été administré à un nombre total de 336 malades. Des types d'expectorations mucoïdes propres à l'examen cytologique furent recueillis dans 88,5% de la totalité du groupe. La production d'expectoration dans 86% des cas, sur 180 malades chez lesquels on n'avait pu mettre en évidence une affection pulmonaire, et qui n'avait ni toux ni expectoration spontanée, fut d'un intérêt particulier, pour permettre le diagnostic cytologique de cancer pulmonaire. On observa chez trois sujets seulement de ce groupe une irritation légère lors de l'inhalation de l'aérosol chaud contenant 10% de sel.

Les études cytologiques sur l'expectoration recueillie chez 74 malades après inhalation de solution à 10% de sel, montrèrent que 79% des spécimens d'expectoration furent satisfaisants pour le diagnostic. Chez cinq malades sur 8 qui étaient atteints de cancer pulmonaire métastatique ou primitif prouvé, les expectorations montrèrent l'existence de cellules malignes. Il n'y eut aucun cas d'erreur. Comme tous les examens furent pratiqués sur un simple échantillon, il est évident que l'étude cytologique d'échantillons multiples obtenus dans des conditions semblables pourrait augmenter les possibilités d'un diagnostic précis. Notre cytologiste exprime l'opinion que cette méthode d'obtenir une expectoration pourrait amener à mettre en évidence des cellules tumorales chez des individus sans symptômes, avant qu'une expectoration spontanée ne survienne, étant donné que les échantillons obtenus par aérosol salin hypertonique se prêtent parfaitement à l'étude.

ZUSAMMENFASSUNG

Es wird berichtet über eine Methode zur Gewinnung von Sputum aus dem Respirationstrakt von "normalen" Individuen, Patienten mit chronischen nicht tuberkulösen Lungenkrankheiten und Patienten mit bekannten oder als solche angenommenen bösartigen Veränderungen. Die Grundlage dieses Vorgehens macht die Inhalation von warmen, hygroskopischen Salz-Aerosolen notwendig.

Ungefähr 10 ccm einer 10-oder 15% Salz-Aerosol-Lösung, die 20% Propylen-Glycol enthielt, wurde insgesamt bei 336 Personen angewandt. Für die cytologische Untersuchung geeignete Schleimhaltige Sputumpräparate wurden in 88,5% der ganzen Serie gewonnen. Von speziellen Inter-

esse als eine mögliche Suchtechnik zur cytologischen Diagnose des Lungenkrabses war das Zustandekommen von Auswurf bei 86% von 180 Personen, bei denen kein Anhalt für eine Lungenkrankheit bestand, also auch kein Husten und auch kein spontaner Auswurf. Nur 3 Personen aus dieser Gruppe bemerkten eine leichte Reizung bei der Inhalation der warmen 10%igen Salz-Aerosol-Lösung.

Cytologische Untersuchungen aus dem Sputum, das von 74 Personen nach der Inhalation von 10% Salzlösung gewonnen war, zeigte, dass 79% der Präparate zur Diagnose ausreichend waren. Bei 5 der 8 Patienten mit nachgewiesenem primären oder metastatischen Lungenkrabs waren die Sputumpräparate positiv hinsichtlich Tunorzellen. Es gab keine irrtümlich negativen Befunde. Da alle diese Untersuchungen mit jeweils einem einzigen Präparat durchgeführt wurden, ist es augenscheinlich, dass cytologische Studien von mehrfach wiederholtem Untersuchungsmaterial das in ähnlicher Weise gewonnen wurde, die Möglichkeiten einer genauen Diagnose erhöhen könnte. Nach der Meinung unseres Zellspezialisten (E.E.S.) kann man von dieser Methode der Sputumgewinnung erwarten, dass sie Tumorzellen zum Nachweis bringt bei erscheinungsfreien Personen, ehe Spontansputum entsteht, da die Präparate, wie sie mit hypertonischer Salz-Aerosol-Lösung erzielt werden, für die Untersuchung völlig ausreichen.

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Chronic Pneumonitis Simulating Bronchiogenic Carcinoma

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Although there has been an improvement in the mortality, morbidity, and five year survival rates for those undergoing operative procedures for cancer of the lung, there are many afflicted with the disease who reach the thoracic surgeon too late for satisfactory surgical therapy, the only accepted curative method available today. All members of the medical profession concerned with this problem realize that a more aggressive approach is necessary in certain clinical conditions.[1-2] "Recurrent" or "unresolved" pneumonias fall in this latter group. The inflammatory reaction may result from intermittent or persistent obstruction of bronchial secretions due to neoplasm or its associated pathology.

Experience with several patients, who were suspected of having bronchiogenic carcinoma, demonstrated the need for conservatism in such cases.

Case 1: A. B., a 66 year old Negro, was admitted to the hospital with a small, firm, slightly movable mass at the vertex of the scalp. This had increased in size during the preceding eight months until it measured 2 x 1.5 cm. Physical examination was otherwise not significant. Hematological determinations were normal except for the sedimentation rate of 34 mm. Smears of three sputum specimens were negative for tuberculi bacilli. The blood serology was positive, but that of the spinal fluid was negative. Roentgenograms of the thorax, postero-anterior (Fig. 1) and right lateral views, revealed a density extending from the hilum into the right lung field with overlying pleural reaction anteriorly.

History of cough, of right anterior chest pain for 18 months, and twelve pound weight loss was elicited. Bronchoscopy revealed no abnormality. Aspirated bronchial secretions utilizing paraffin sections (of cell blocks) were negative for tumor cells. The scalp lesion was excised and reported as an epidermal inclusion cyst. Several loose teeth were removed. The usual pre-operative routine was completed except that 300,000 units of penicillin were given twice daily for 12 days because of the positive blood serology. At operation adhesions were found extending from a firm mass in the upper and middle lobes of the right lung to the anterior chest wall and to the mediastinum. Pneumonectomy was performed.

The specimen consisted of the right lung weighing 500 grams. The segmental bronchi of the middle lobe and anterior segment of the upper lobe were stenosed and surrounded by a firm mass, 8 x 6.5 x 6 cm. The fairly dry lesion consisted mostly of grayish-green tissue which extended antero-laterally. At only one point was the overlying pleura dimpled and attached. The remainder of the lung parenchyma was not remarkable except for congestion due to surgery and apical subpleural emphysematous blebs. Microscopic examination revealed many macrophages with oval, eccentrically placed nuclei and many small vacuoles (stained with Scarlet Red) in the cytoplasm. These cells were seen in the areas of acute and chronic inflammation. The pathologist reported chronic pneumonitis, cholesterol type.

His condition during and following operation was satisfactory. During a period of 17 months he had three follow-up visits. Roentgenograms

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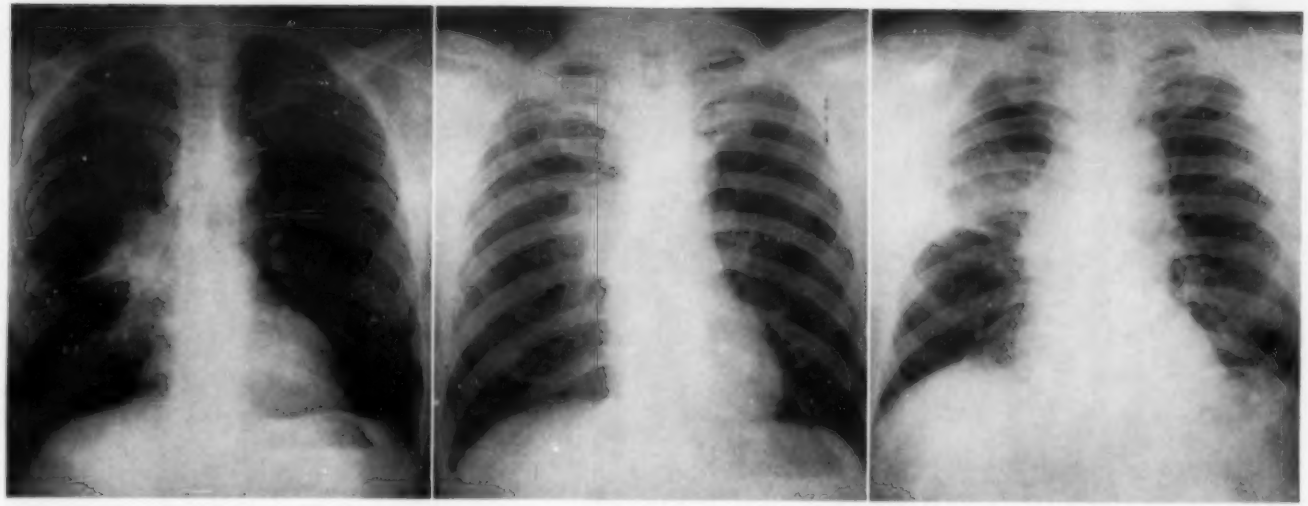

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1 (Case 1): Roentgenogram showing hilar mass extending into the right lung field suspicious of bronchiogenic carcinoma.—*Figure 2* (Case 2): Roentgenogram showing right hilar mass characteristic of carcinoma of the lung.—*Figure 3* (Case 3): Roentgenogram showing mass in right upper lobe suspicious of bronchiogenic carcinoma.

revealed the mediastinal structures markedly deviated to the right with some herniation of the well aerated, normal left lung through the mediastinum. The right hemithorax was opaque. Vital capacity was 45.7 per cent of normal, and maximum breathing capacity was 31 per cent of normal. The immediate post-operative dyspnea diminished. He had gained nine pounds in weight and was able to work as a janitor when last seen.

Case 2: J. J. W., a 41 year old Negro, landscape gardener, was transferred from another hospital with a cough productive of clear mucoid sputum for one year. Within the past three months two teeth had been extracted. Because of weakness he had discontinued work. Two episodes of hemoptyses, each of which included more than a cupful of blood, and was precipitated by coughing, occurred respectively one week and two days before admission. Dyspnea was noted after the first episode. After the second hemoptysis a roentgenogram was taken and he was told of a "growth" in the right lung. Additional questioning disclosed some right chest pain and occasional expectoration of foul-smelling sputum.

Physical examination revealed several missing teeth and others in poor condition, limitation of motion of the right hemithorax, and dullness posteriorly in the right mid-thoracic area with breath sounds diminished over the same area. His hemoglobin was 11.5 grams. Tubercle bacilli were not found in smears of two sputum specimens. A roentgenogram (Fig. 2) revealed a density in the right hilar region which extended laterally and anteriorly to the pleural surface.

Bronchoscopy was performed without significant pathological findings. Bronchial secretions were negative for tumor cells. Thoracotomy revealed a firm palpable mass in the anterior contiguous portions of the upper and middle lobes of the right lung. Bilobectomy was done. Frozen section of the specimen revealed no neoplastic tissue.

The specimen consisted of the upper and middle lobes of the right lung weighing 236 grams. The pleura was smooth except for an area of scarring over the latero-posterior surface. In this area lying on both sides of the fissure, approximately 4 cm. from the periphery of the lung, was a firm rounded, fairly discrete grayish mass measuring 6 x 4.5 x 2.5 cm. Its center contained an area of cavitation (1.5 cm. in diameter) which had an ill defined wall covered by a shaggy exudate. The remainder of the specimen was crepitant to palpation. Lymph nodes about the upper and middle lobe bronchi were small, soft and anthracotic.

Microscopical sections of the mass showed interstitial chronic reaction and fibrosis. The overlying pleura was thickened by numerous dilated vessels and loose edematous fibrous tissue. Cells with clear or foamy refracticle cytoplasm were present in many scattered areas. An abscess with cavitation was in the center of the lesion surrounded by large areas of organizing pneumonia. The alveoli, in a few focal areas, contained refractile vacuoles and macrophages with numerous small vacuoles giving them a foamy appearing cytoplasm. On proper staining the macrophages were seen to contain fat. Sections of lymph nodes revealed hyperplasia, hyperemia, mild anthracosis, and edema. The pathologist diagnosed chronic pneumonitis with a cavitating abscess of the right upper and middle lobes.

During and following surgery his course was uneventful and he was discharged on the 12th postoperative day.

Two months after discharge he reported seven pounds gain in weight. Physical and roentgenological examinations disclosed no abnormality of the remaining lung. Four days later he had evidence of jaundice. He was readmitted to the hospital and gave a history of two previous episodes

of "yellow jaundice." After clinical and laboratory studies resulted in the diagnosis of acute hepatitis due to homologous serum jaundice, treatment was initiated with satisfactory results.

Seven months after operation his vital capacity was 3,000 cc. (60 per cent of normal). Laboratory examinations revealed no evidence of hepatitis. One year after operation he had gained 50 pounds and was attending school.

Case 3: L. R., a 54 year old laborer, was transferred from another hospital with the diagnosis of pneumonitis and bronchiogenic carcinoma of the right lung. Two months previously he had noted the onset of lassitude and inability to work two consecutive days because of fatigue. One month later dyspnea and anorexia were noted as well as knife-like right upper chest pain aggravated by coughing. In addition he had lost 10 pounds in weight. Cough productive of yellow, tenacious sputum developed. He was admitted to the other hospital because of fever. Aureomycin was discontinued after eight days because of marked improvement. A relapse occurred five days later and aureomycin was initiated again for eight more days. At intervals roentgenograms of the chest strongly suggested bronchiogenic carcinoma. Bronchoscopy was performed, and the aspirated secretions were interpreted as compatible with primary carcinoma, undifferentiated type.

Physical examination revealed alopecia of the left parieto-occipital region, carious teeth and pyorrhea, diminished breath sounds and occasional fine rales over the right upper anterior thorax, and exostosis of the right first metatarso-phalangeal joint. His pulse rate was 100 and blood pressure 170/100.

Hematological, serological, and chemical examinations were unrevealing. Several sputum examinations were negative for tubercle bacilli. Roentgenograms (Fig. 3) showed a hazy indistinct infiltration of the anterior portion of the upper lobe to the right. Comparison with roentgenograms previously made revealed that originally a much larger area of infiltration had been present. The radiologist interpreted the findings as consistent with the diagnosis of bronchiogenic carcinoma.

After a review of the clinical and laboratory data the parenchymal process was considered inflammatory. However, considering his age, and the relatively large amount of residual inflammation, exploratory thoracotomy was considered obligatory. Bronchoscopy and bronchial secretions showed no evidence of neoplasm.

At thoracotomy a firm mass in the anterior portion of the upper lobe of the right lung was found adherent to the chest wall and mediastinum by firm thick vascular adhesions. A firm lymph node located inferior to the axygos vein, and several small pieces of the mass were removed, which were negative for neoplasm. *Only the anterior segment* of the right upper lobe was removed. The pathologist reported that this specimen showed chronic fibrosing pneumonitis.

The segmental bronchus appeared entirely normal. The peribronchial tissue was moderately firm and upon section appeared to be replaced by dull gray fibrous tissue. In no area was there evidence of neoplasm, cyst, or abscess. The accompanying lymph node appeared normal in size and consistency on viewing its surface. Microscopic examination revealed a large ganulomatous area consisting of interlacing bands of fibrous tissue containing a few scattered lymphocytes and an occasional polymorphonuclear leukocyte. There were giant cells in which 3 or 4 nuclei were arranged centrally or peripherally. No areas of necrosis were seen. The overlying pleura was greatly thickened by dense hyalinized fibrous tissue in which there were a few small vessels. In some sections there were discrete areas in which the pulmonary parenchyma was entirely replaced by fibrous tissue. In these areas there were numerous lipophages and foci of acute and chronic inflammation. No evidence of malignancy was seen. Examination of the lymph node from the region of the right main stem bronchus revealed a mild lymphoid hyperplasia and a moderate amount of anthracotic pigment. The pathologist reported chronic pneumonitis, etiology undetermined, in the segment of lung removed.

The postoperative course was uneventful and he was discharged.

One month later he was readmitted for excision of the exostosis of the first metatarso-phalangeal joint. Roentgenograms revealed no evidence of disease then or one year later when he reported that he was well.

Discussion

How *aggressive* should the medical profession be in the management of patients who roentgenograms reveal evidence of persisting pulmonary lesions suggesting bronchiogenic carcinoma? Clinicians who reviewed the preoperative clinical, roentgenological, and laboratory findings in these three cases did not hesitate to recommend surgery inasmuch as they could not be certain that carcinoma did not exist. Bronchoscopy, cardiorenal tests, and the patient's general condition did not contraindicate thoracotomy in any of them. In the operating room gross appearance and palpation were found to be insufficient criteria for definitive diagnoses. The Pathology Department assumed responsibility for the histological diagnosis by doing frozen sections at the time of operation in the last two cases. Thus, the aggressive attitude of clinicians combined with the judgment of surgeons and pathologist results in better care of the patients. Undoubtedly an aggressive policy indicates that more clinicians who see patients with persistent signs and symptoms of pneumonitis should request serial roentgenograms. If this is done, more pulmonary pathology, including early cases of carcinoma of the lung will be recognized.

How long should one observe or treat medically a patient with pneumonitis (viral or atypical, unresolved or recurrent)? Experience with two other patients each of whom had a small bronchiogenic carcinoma obstructing a segmental bronchus demonstrated that one should not observe patients for long periods without taking action. The first patient, a 56 year old negro, had a cough and anorexia for one month preceded by some weakness and loss of weight. Although bronchoscopy was negative, serial roentgenograms, during one month of observation, demonstrated recurrence of segmental atelectasis and pneumonitis of the right upper lobe. The second patient, a 75 year old man, had had initial symptoms of chills and fever three months previously and was treated elsewhere for pneumonia. Subsequently he had developed weakness and loss of weight and was admitted to another hospital. It should be noted that he always had chronic cough; however, it became more productive and was intermittently sanguinous after the onset of the above symptoms. During the evaluation of complaints referable to the genitourinary and gastrointestinal systems he had another episode of pneumonitis. This was demonstrated by increase in the disease of the upper lobe of the left lung as seen on roentgenograms. Each of these patients had upper lobectomy.

Since patients should be evaluated individually, one cannot safely propose general rules for all. One may conclude, however, that it is unwise to postpone exploratory thoracotomy more than eight weeks in a 35-40 year or older person who has unresolved or recurrent pneumonia, or lobar

or segmental atelectasis, unless there is a contraindication. This type of management is especially advised if the patient is a man, has been a heavy smoker, or has significant symptoms.

Frequently the attending physician will prolong the diagnostic and observation period in cases of "pneumonitis," which have thoracic roentgenograms suggestive of carcinoma of the lung, and thus delay operative intervention too long. The results of laboratory tests made over a long period of time may be misleading and also indecisive. A negative result of the study of sputum, or bronchial secretions, does not necessarily rule out a malignant pulmonary lesion. Likewise a positive test may be erroneous (Case 3). Cases are known in which total pneumonectomy was done because of a positive Papanicolaou test of bronchial secretions or sputum; in two cases the pathologists found no evidence of a malignant lesion in the surgical specimen.

How far should a *conservative* policy be carried by the surgeon? After experience with Case 1 it was decided to have a histological diagnosis (of the pathological pulmonary tissue) before any significant resection was done. As a result more limited excisions were performed in Cases 2 and 3. This proved wise for no neoplastic process was present in the surgical specimens. Larger resections would have unnecessarily removed some functioning pulmonary tissue and would have been too radical. Conservative management, especially in the third patient, where a diagnosis of bronchiogenic carcinoma had been made elsewhere, was of value to the patient.

A number of authors have contributed to the development of the policy of *aggressive conservatism*. Paulson and Shaw[1] emphasized the significance of pneumonitis in a study of 362 patients with bronchiogenic carcinoma. They found viral or atypical pneumonias and unresolved pneumonia to be two of the commonest erroneous diagnoses which contributed to the delay in treatment. Ochsner *et al*[2] reported that a lower respiratory tract infection was frequently the earliest manifestation of a bronchiogenic carcinoma. In their series of 948 patients, 55 per cent gave histories of previous respiratory tract infection diagnosed either as influenza, viral pneumonia, or non-specific pneumonitis. Such an infection was the first manifestation in 22 per cent of their patients. After their recovery from pneumonitis there were persistent symptoms! Freedlander and Wolpaw[3] and Adams,[4] urged resection of inflammatory lesions of the lung because of the difficulty in differentiation from carcinoma. In a classic article, Waddell, Sniffen and Sweet[5] reported that six of 10 cases of chronic pneumonitis had a preoperative diagnosis of carcinoma of the lung. There is, then, much evidence that good judgment is needed in the management of such cases.

SUMMARY AND CONCLUSIONS

In cases of viral, or atypical, and unresolved or recurrent pneumonias, with persistent roentgenological findings suggestive of carcinoma of the lung, the attending physician should consider consulting a well trained

thoracic surgeon concerning the advisability of thoracotomy for diagnostic and therapeutic purposes.

The surgeon responsible for such a patient cannot depend entirely on the results of laboratory studies of bronchial secretions and sputum. At the time of operation his decision concerning the amount of pulmonary tissue to be resected should be based on a pathological examination of an adequate biopsy of the diseased tissue.

Experience with three patients with suspicious thoracic roentgenological findings illustrates the advisability of a policy of *aggressive conservatism*.

RESUMEN Y CONCLUSIONES

En casos de neumonías, de virus, o atípicas y neumonías no resueltas o recurrentes con hallazgos radiológicos sugestivos de carcinoma del pulmón, el medio tratante debe considerar la necesidad de consultar con un cirujano de tórax bien preparado respecto de la toracotomía con fines diagnósticos y terapéuticos.

El cirujano responsable de tales enfermos no puede fiarse enteramente de los estudios de laboratorio de las secreciones bronquiales y del esputo. Durante la operación su decisión respecto de la cantidad de pulmón que ha de resecarse debe basarse en el examen histopatológico con biopsia adecuada.

La experiencia en tres enfermos con hallazgos roentgenológicos sospechosos a los rayos X ilustra lo aconsejable que es una actitud *conservadora agresiva*.

RESUME

En présence de pneumopathies à virus, ou de pneumonies atypiques, et des formes résistantes au traitement ou donnant lieu à une rechute, avec constatations radiologiques persistantes, évocatrices de carcinome pulmonaire, le médecin traitant devrait envisager de consulter un chirurgien thoracique bien expérimenté sur la nécessité de pratiquer une thoracotomie dans un but diagnostique et thérapeutique.

Le chirurgien responsable d'un tel malade ne peut pas se fier entièrement aux résultats des études de laboratoire des sécrétions bronchiques et des expectorations. Au moment de l'opération, sa décision concernant la quantité de tissu pulmonaire qui doit être réséquée devrait être basée sur l'examen anatomo-pathologique d'une biopsie bien exécutée du tissu atteint.

L'auteur rapporte le cas de trois malades pour lesquels les constatations radiologiques thoraciques étaient suspectes et qui illustrent l'opportunité d'un programme de "conservatisme agressif."

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

In Fällen Viruspneumonien oder atypischen und ungeklärten oder rezidivierenden Pneumonien mit auf Lungencarcinom verdächtigen beständigen röntgenologischen Befunden muss der behandelnde Arzt in Erwägung ziehen, einen gut erfahrenen Thorax-Chirurgen zu konsultieren hinsichtlich der Zweckmässigkeit einer Thorakotomie aus diagnostischen und therapeutischen Gründen.

Der für einen solchen Kranken verantwortliche Chirurg kann nicht ganz abhängig sein von den Ergebnissen von Laboratoriums-Untersuchungen von Bronchialsekreten und Sputum. Zum Zeitpunkt der Operation muss sich seine Entscheidung hinsichtlich des Ausmasses von zu resezierendem Lungengewebe stützen auf eine pathologisch-anatomische Untersuchung einer adaequaten Biopsie des erkrankten Gewebes. Erfahrung mit 3 Patienten mit verdächtigen Thorax-Röntgenbefunden erläutert die Zweckmässigkeit einer Methode des *agressiven Konservativismus.*

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Cycloserine-Isoniazid Combination Therapy in Virgin Cases of Pulmonary Tuberculosis

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Cycloserine* (CS) is an antibiotic produced by *Streptomyces orchidaceous*.[1] It is of low molecular weight, and is readily soluble in body fluids. The determination of CS in body fluids has been facilitated by the chemical method devised by Jones.[2] Cycloserine has been shown to penetrate readily into the body cavities, and to be excreted in the sputum, saliva, urine, bile, and mother's milk. It also enters the spinal fluid and the fetal blood by way of the placenta.[3, 4] Although CS is a broad-spectrum antibiotic,[5-8] its primary usefulness has been established in the treatment of tuberculosis.[9] It is excreted into the urine in high concentrations,[5] and has been found useful in the treatment of urinary infections.[8]

Against the tubercle bacillus, CS is effective *in vitro* in higher concentrations than those obtained with isoniazid (INH) or streptomycin.[5, 10] However, its easy absorption into the blood stream[5] and virtually universal distribution into the tissues[3] results in higher plasma and tissue concentrations than is the case with other antituberculosis agents. For this reason, although CS is less effective than INH *in vitro*, the clinical dose is approximately the same, i.e., 5 to 10 mg./Kg. of body weight per day.

Cycloserine has been shown to be effective in previously untreated cases of tuberculosis, but has proved especially useful in chronic, resistant cases.[9, 11-14] In addition, it will be shown in this presentation that sensitivity of the tubercle bacillus during treatment with CS falls rather slowly, and seldom reaches serum concentrations that cannot be attained clinically.[15] True resistance to CS develops but rarely, if at all.

Cycloserine-Isoniazid Combination Therapy in Tuberculosis

The upper limits of CS dosage are set by the neuropsychiatric symptoms which sometimes develop during continued administration. These will be discussed in detail and related to plasma concentrations of CS in another report. Some data on CS-INH combination therapy have been presented in preliminary and interim reports.[15, 16] Details of the

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*Manufactured by Commercial Solvents Corporation, Terre Haute, Indiana, and marketed by Eli Lilly and Company, Indianapolis, Indiana as 'Seromycin' (Cycloserine, Lilly).

FIGURE 1A FIGURE 1B FIGURE 1C

FIGURE 1: Patient D. L., a 22 year old Puerto Rican woman, was admitted with a two weeks' history of loss of weight, anorexia, night sweats, and cough. Admission sputum showed tubercle bacilli on smear, and x-ray film of the lungs revealed a caseous pneumonic lesion of the right upper lobe (Fig. 1A). She was started on cycloserine, 0.25 Gm. and isoniazid, 0.15 Gm. twice daily. There was prompt and marked symptomatic improvement. After six weeks of therapy, the sputum and gastric contents were devoid of tubercle bacilli on smear and culture. Serial x-ray films showed slight improvement on the sixth week, moderate improvement on the 17th (Fig. 1B) and 24th weeks, and marked improvement on the 26th week (Fig. 1C) of therapy. She gained 52 lb. in weight during her hospital stay. After six months of hospitalization, she was discharged to the Out-patient Clinic and continued on the combination therapy.—*Figure 1A:* X-ray film of the lungs taken on admission shows a caseous pneumonic lesion in the right upper lobe.—*Figure 1:* X-ray film taken after 17 weeks of therapy shows moderate improvement of the right upper lobe lesion.—*Figure 1C:* X-ray film taken after 26 weeks of therapy shows almost complete clearing of the right upper lobe.

clinical procedure used during this study will therefore not be presented here.

No randomization was attempted, but all subjects entering our service at the Metropolitan Hospital were treated with a combination of CS, 0.5 Gm./day, and INH, 0.3 Gm./day, divided in two doses and given morning and evening. In addition to the usual routine observations, an x-ray film of the chest was made monthly, bacterial examination of the sputum was made bimonthly by smear and culture, and when negative, of the gastric contents. Cycloserine plasma levels were obtained at regular intervals, and as dictated by the clinical progress and the appearance of side reactions. Liver and kidney function tests and peripheral blood studies were also done several times during the study.

When tubercle bacilli were isolated from the sputum or gastric contents, they were subjected to routine sensitivity determinations to CS and INH, according to the standards recommended by the VA.[18] These data have been referred to elsewhere,[15] and will be presented in detail in a later report.

Results

As of February 1, 1957, there were 81 patients on the CS-INH combination for from six weeks to 16 months. The dose was CS, 0.25 Gm. and INH, 0.15 Gm., given orally, twice daily. The pretreatment data on these patients are shown in Tables I and II. The severity and acuteness of the tuberculous process is attested to by the fact that 84 per cent of the patients had some degree of fever. Very few early cases are admitted to this hospital, and that is the reason for the low number with minimal x-ray film evidence of disease. All sputa were positive for tubercle bacilli on smear, and confirmed by culture. Presumably, none of the subjects had been treated with antimicrobial agents prior to admission.

Table II shows the x-ray film estimate of pulmonary involvement before the onset of therapy, using the criteria recommended by the National Tuberculosis Association. X-ray film evidence of progress during treatment is shown in Table III. About 40 per cent of the x-ray films showed evidence of improvement within six weeks of treatment. The figure rose to 74 per cent of 74 subjects treated for 12 weeks, and, within six months, to 93 per cent of the 48 remaining subjects.

TABLE I

CYCLOSERINE COMBINATION THERAPY
PULMONARY TUBERCULOSIS
Cycloserine 0.5 Gm. plus INH 0.3 Gm./day, orally

81 Cases			Age: 17-73 Years (Av. 38)	
Sex:	Male 55	Female 26		
Race:	White 23	Negro 30	Puerto Rican 24	
			Others 4	

FIGURE 2A FIGURE 2B FIGURE 2C

FIGURE 2: Patient K. S., a 35 year old white woman, was admitted with a two months' history of productive cough, weight loss, anorexia, and night sweats. Admission sputum showed tubercle bacilli on smear, and an x-ray film revealed fibrocavitary tuberculosis involving the entire left lung, with a large cavity in the left upper lobe (Fig. 2A). She was started on cycloserine, 0.25 Gm. and isoniazid, 0.15 Gm. twice daily. After 12 weeks of therapy, the sputum and gastric contents were devoid of tubercle bacilli on smear and culture. Serial x-ray films revealed minimal improvement by the sixth week, moderate improvement by the 18th week (Fig. 2B), and marked improvement by the 36th week (Fig. 2C) of therapy. The patient showed symptomatic improvement and gained 34 lb. during her seven months' stay in the hospital. She was then discharged to the Outpatient Clinic and continued on the combination therapy.—*Figure 2A:* X-ray film taken on admission shows an extensive fibrocavitary tuberculosis involving the entire left lung with a large cavity in the left upper lobe, and minimal involvement of the right lobe.—*Figure 2B:* X-ray film taken after 18 weeks of therapy shows moderate improvement of the extensive pneumonic disease in the left upper lobe, and clearing of the right lung.—*Figure 2C:* X-ray film taken after 36 weeks of therapy shows marked reduction of the tuberculous process in both lungs. There is no evidence of the cavity which was present on admission.

There was prompt reduction in the bacillary content of the sputum, as shown in Table IV. At the same time, cough diminished and the amount of sputum lessened and became less purulent. Only those sputa and gastric contents are reported as negative which showed absence of tubercle bacilli on both smear and culture. Within three months, 80 per cent of 64 sputa were bacteriologically negative, and at six months the figure rose to 87 per cent of the sputa. That CS may be presumed to have played a major role in the attainment of these results, is shown by our own data on the treatment of chronic, resistant tuberculosis with CS, 0.5 Gm./day,[13] as well as by the results of others.

Moyer, *et al.*[19] obtained similar data on the sputa of original treatment cases receiving CS alone, 0.5 Gm./day. Within two months of treatment, nine of 12, and at three months, nine of 11 subjects showed sputa negative for tubercle bacilli. Cummings,[20] on data pooled from 10 Veterans Administration Hospitals, reported 35 per cent negative cultures at two months, 61 per cent at four months, and 74 per cent at six months of treatment of original cases of tuberculosis with CS alone, 1.0 Gm./day. Therefore, we feel justified in assigning an important role to the part played by CS in our series of CS-INH combination therapy, and Moyer, *et al.*[19] concluded that, "Cycloserine appears to be of value in the treatment of tuberculosis even at a reduced dosage of a 0.5 gram daily." Isoniazid alone could not account for our results, according to our own unpublished experience. In addition, Russell, *et al.*[21] using INH alone in daily doses of 3.0 to 5.0 mg./Kg. on 286 patients, reported that, ". . . only 37 per cent were bacteriologically negative at four months of therapy; 45 per cent were excreting INH-resistant tubercle bacilli."

Sensitivity tests showed a slight decrease of bacillary sensitivity when the dose of CS was 1.0 Gm. or more per day. However, from 0.5 Gm./day of CS there was no evidence of decreased sensitivity. Our data, which will be detailed elsewhere, show that "resistance" to CS did not develop, and that the slow and slight drop in sensitivity from the larger doses of CS was not sufficient to interfere with prolonged therapy. Moyer, *et al*[19] reported data similar to ours, in that only one out of 40 subjects produced bacilli which became insensitive to 40 mcg./ml. of CS. From the use of only 0.5 Gm./day of CS, these authors obtained blood levels of CS which were ". . . between 10 and 30

TABLE II

CYCLOSERINE COMBINATION THERAPY
PULMONARY TUBERCULOSIS

Stage of Disease:	Far Advanced	28
	Moderately Advanced	51
	Minimal	2
X-ray Appearance:	Caseopneumonic	24
	Fibrocavitary	57
No. of Patients with Temperature at Start of Therapy: Range: 105° to 99° F.—Average: 100.8° F.		68

mcg./cc., the majority being between 20 and 30 mcg./cc." and their data agree with those of Cummings,[20] and with our own. It is therefore difficult to see how one can ascribe clinical "resistance" to patients with plasma levels of CS of between 20 and 30 mcg./cc. when the tubercle bacilli are inhibited by similar levels of CS *in vitro*.[19] However, we feel that the data are not in accord with the conclusion of Moyer, *et al.*[19] that, "Bacterial resistance to cycloserine occurs rapidly and at about the same degree as that observed when streptomycin or INH is used alone."

Most of the cases treated for more than one month showed rapid development of resistance to INH. These data are not complete, but agree with those of Schwartz and Moyer[22] on the use of INH alone. It appears that CS does not delay the emergence of resistance to INH when the two drugs are administered simultaneously.

Toxic symptoms occur but rarely from 0.5 Gm. of CS per day, alone or in combination with INH.[16, 24-28] From doses of 1.0 Gm. or more per day, the toxicity observed is referable to the central nervous system. These data will be presented elsewhere, and correlated with plasma levels and background conditions, such as inanition, alcoholism, epilepsy, etc. Progress in the study of the origin of these symptoms has been handicapped by the so-called "cycloserine paradox"[29] which extends both to the tuberculous process and to the toxicity, i.e., animals are not readily susceptible to either the antituberculosis or toxic effects of CS[17, 23, 32] as manifested clincally in patients.

Discussion

After establishing proof that CS alone was efficaceous in the treatment of tuberculous subjects, there remained a number of areas for further investigation. One of these is the subject of this report, namely, the effects of therapy with a combination of CS and INH or streptomycin. The results of a preliminary study[16, 25] indicated an additive and possibly synergistic effect between CS and INH, while the results from the CS and strepto-

TABLE III

CYCLOSERINE COMBINATION THERAPY
PULMONARY TUBERCULOSIS
X-Ray Status

	Period (months)				
Degree of Change	1½	3	6	9	12
Marked Improvement	1	12	20	12	6
Moderate Improvement	32	43	25	7	2
Slight to No Change	46	17	3	0	0
Worse	2	2	0	2	0
TOTAL	81	74	48	21	8

mycin combination were inferior. The relatively small number of cases makes it difficult to compare the effects of CS-INH with the usual INH-PAS combinations. However, the clinical results so far obtained by us, and confirmed by Robitzek and Nenashev[14] are consistent with the fact that the CS-INH regimen represents the combination of two potent antituberculous agents, rather than the mere enhancement of the action of INH, as is true for PAS. Toxicity has posed no problem when 0.5 Gm. of CS is used alone or combined with INH, despite the administration of two drugs with somewhat similar neurotoxic effects. Prescott, *et al.*[30] have demonstrated an increased tolerance to INH in mice by the use of CS.

Our impression of synergistic action between CS and INH is supported by the findings of Cummings, *et al.*[10] *in vitro*, and by the results of Schmidt[31] on monkeys, and of Wolinsky and Steenken[17] on guinea pigs. The latter showed that non-antituberculous doses of CS enhanced the therapeutic effects of INH.

SUMMARY AND CONCLUSIONS

1. New, previously untreated cases of pulmonary tuberculosis were treated with a cycloserine-isoniazid combination given orally.

2. Eighty-one cases have been treated for from six weeks to 16 months, with but a single reaction, which did not necessitate discontinuance of treatment.

3. Clinical improvement, reduction of fever, lessening of the volume of sputum, and gain in weight occurred promptly in every case. In addition, the administration of a single capsule containing cycloserine and isoniazid, twice daily, was more acceptable to the patients than the usual INH-PAS combination.

4. Within six weeks, 40 per cent of the x-ray films showed evidence of improvement. The figure rose to 74 per cent in 12 weeks, and to 93 per cent of 48 subjects treated for six months.

5. Evidence of reduction in the bacillary content of the sputum was

TABLE IV

CYCLOSERINE COMBINATION THERAPY
PULMONARY TUBERCULOSIS
Bacteriological Status

Initially all sputa were strongly positive on smear and culture

	Period (Months)				
Degree of Change	1½	3	6	9	12
Negative	37	51	29	10	6
Positive	38	13	6	4	0
Pending	6	10	13*	7*	2*
TOTAL	81	74	48	21	8

*All of these were negative on culture previously.

obtained within six weeks of treatment. Within three months, 80 per cent of 64 sputa were negative on culture, and at six months the figure rose to 87 per cent.

6. Bacillary sensitivity to cycloserine fell slowly and slightly during prolonged treatment with the larger doses. From 0.5 Gm. of cycloserine per day, there was no evidence of decreased sensitivity.

7. Resistance to INH developed during the administration of the cycloserine isoniazid combination at approximately the same rate as is seen when INH is given alone.

8. It is our conclusion that a combination of 0.25 Gm. of cycloserine and 0.15 Gm. of INH given twice daily is effective and safe therapy against previously untreated cases of pulmonary tuberculosis. We feel that our clinical results were superior to the usual INH-PAS therapy, both in speed and degree of response, as gauged by x-ray film changes and sputum conversion.

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RESUMEN Y CONCLUSIONES

1. Se trataron casos nuevos sin haber recibido previamente otro tratamiento, con la asociación de cicloserina-isoniacida, oralmente.

2. Se han tratado ochenta y un casos por seis a 16 meses con sólo una reacción que no necesitó interrupción del tratamiento.

3. Mejoría clínica, reducción de la fiebre, disminución del volumen de los esputos, y aumento de peso, fué lo que ocurrió en todos los casos. Además, la administración de una sola capsula conteniendo cicloserina e isoniacida, dos veces al día, fué más aceptable para los enfermos que la combinación habitual de PAS-HAIN.

4. Dentro de seis semanas el 40 por ciento mostraron mejoría radiológica evidente. Subió la proporción a 74 por ciento a las 12 semanas y a 93 por ciento de 48 sujetos tratados por seis meses.

5. Se logró evidencia de reducción del contenido bacilar de los esputos dentro de seis semanas. Dentro de tres meses, 80 por ciento de 64 esputos fueron negativos al cultivo, y a los seis meses subió a 93 por ciento.

6. La sensibilidad bacilar a la cicloserina cayó lenta y ligeramente durante tratamiento prolongado a altas dosis. Usando 0.5 de cicloserina por día, no se observó decrecimiento de la sensibilidad.

7. La resistencia a la HAIN se observó durante la administración de cicloserina-HAIN en la misma proporción que ocurre con la isoniacida sola.

8. Concluimos que una combinación de 0.25 de cicloserina y 1.15 Gm. de HAIN dados dos veces al día, es un tratamiento seguro y efectivo contra los casos nuevos de tuberculosis. Creemos que nuestros resultados son superiores a los logrados con PAS/HAIN usual tanto en rapidex como en grado de respuesta según puede estimarse por el aspecto radiológico y la conversión de esputos.

RESUME

1. Des formes de tuberculose pulmonaire récente, sans traitement préalable, furent traitées par l'association cyclosérine-isoniazide administrée par voie buccale.

2. 81 cas ont été traités de six à 16 mois, avec une seule réaction qui ne nécessita pas la cessation du traitement.

3. L'amélioration clinique, l'abaissement de la fièvre, la diminution du volume de l'expectoration et le gain de poids corporel survinrent rapidement dans chaque cas. En outre, l'administration d'une seule capsule contenant la cyclosérine et l'isoniazide, deux fois par jour, fut acceptée davantage par les malades que l'association habituelle isoniazide-P.A.S.

4. Au bout de six semaines, 40% des films radiologiques montrèrent une amélioration évidente. Le chiffre s'éleva à 74% pour 12 semaines, et à 93% chez 48 malades traités pendant six mois.

5. La preuve de la réduction du contenu bacillaire de l'expectoration fut obtenu en six semaines de traitement. En trois mois, 80% de 64 expectorations furent négatives à la culture, et au bout de six mois, le chiffre s'éleva à 93%.

6. La sensibilté des bacilles à la cyclosérine s'atténua lentement et faiblement pendant le traitement prolongé avec des doses plus élevées. Pour 0,5 mmgr. de cyclosérine par jour, il n'y eut aucune mise en évidence d'une diminution de la sensibilité.

7. La résistance à l'isoniazide, développée pendant l'administration de l'association de la cyclosérine-isoniazide, est approximativement la même que celle constatée lorsque l'isoniazide est donnée seule.

8. L'auteur conclut que l'association de 0,25 g. de cyclosérine et de 1,15 g. d'isoniazide donnée deux fois par jour est un traitment efficace et sans danger pour les nouveaux cas de tuberculose pulmonaire. Il croit que ses résultats cliniques furent supérieurs à ceux obtenus avec la thérapeutique habituelle par l'isoniazide-P.A.S., à la fois pour la rapidité de la réponse au traitement et son degré, comme le prouvent les modifications radiologiques et la négativité de l'expectoration.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNG

1. Es wurden frische, zuvor unbehandelte Fälle von Lungentuberkulose mit einer per os gegebenen Kombination von Cykloserin-INH-Kombination behandelt.

2. Es wurden 81 Fälle zwischen 6 und 16 Monaten behandelt mit nur einer einzigen Nebenwirkung, die jedoch keine Unterbrechung der Behandlung notwendig machte.

3. Klinische Besserung, Herabsetzung des Fiebers, Verringerung der Auswurfmenge und Gewichtszunahme traten prompt in jedem Falle ein. Zusätzlich war die Verabfolgung einer einzelnen Kapsel mit Cykloserin und INH 2-mal täglich für den Patienten besser zuträglich, als die gewöhnliche INH-PAS-Kombination.

4. Innerhalb von 6 Wochen zeigten 40% der Röntgenaufnahmen einen

Anhalt für eine Besserung. Die Ziffer stieg bis auf 74% in 12 Wochen und auf 93% bei 48 Personen die 6 Monate lang behandelt wurden.

5. Ein Anhalt für die Hersetzung des Bazillengehaltes des Sputums liess sich innerhalb von 6 Behandlungswochen erreichen. Innerhalb von 3 Monaten waren 80% von 64 Sputen kulturell negativ und in 6 Monaten stieg diese Ziffer bis auf 93%.

6. Die bakterielle Sensibilität auf Cykloserin ging langsam und leicht zurück während lang anhaltender Behandlung mit grösseren Dosen. Bei 0,5 Cykloserin täglich fand sich kein Anhalt für eine Herabgesetzte Sensibilität.

7. INH-Resistenz entwickelte sich während der Anwendung der Cykloserin-INH-Kombination in ungefähr der gleichen Häufigkeit, wie man sie sieht, wenn INH allein gegeben wird.

8. Es ist unsere Folgerung, dass eine Kombination von 0,25 Cykloserin und 1,15 INH, 2-mal täglich gegeben, eine wirksame und sichere Therapie ist bei neuen Fällen von Lungentuberkulose. Wir haben den Eindruck, dass unsere klinischen Ergebnisse der gewöhnlichen INH-PAS-Behandlung überlegen sind, sowohl im Tempo wie im Grad der Antwort, wie sich schätzen lässt aus den röntgenologischen Veränderung und dem Negativ-Werden des Sputums.

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Artificial Pneumothorax as an Aid to Chemotherapy in the Treatment of Pulmonary Tuberculosis*

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Twenty years ago, when the writer joined the staff of the Brompton Hospital in London, approximately half the tuberculous patients were having artificial pneumothorax (A.P.) treatment. During the next 10 years there was a slow decline in the use of this method and in the past five years that decline has become more rapid. Figure 1 (Table I) shows the percentage of patients discharged from the Brompton Hospital Sanatorium at Frimley over the past six years who had unilateral A. P. treatment. In 1950 A. P. was attempted in 4 per cent and kept up in 31 per cent, while in 1956 it was attempted in 8 per cent and maintained in only 3 per cent. As most of the patients in this Sanatorium are under the care of physicians on the staff of the Brompton Hospital, these figures reflect the views of a representative group of British Chest Physicians. Individual opinions of course vary considerably; all would agree that A.P. now only has a limited place in the treatment of pulmonary tuberculosis but some have gone further and have ceased to use the method altogether. It is the purpose of this paper to assess the present position and attempt to decide which of these views is right.

Historical Survey

It may help to clarify our ideas if we survey briefly the vicissitudes of A.P. treatment in the past 20 years. At first the selection of cases was poor, with the result that many unsatisfactory pneumothoraces were induced and maintained and the complication rate was high. Gradually the principles underlying successful collapse therapy became apparent, particularly the need for effective relaxation of the diseased area. But, as so often happens, the pendulum swung too far; the pursuit of the free lung became almost a fetish and few patients escaped thoracoscopy. Cauterisation of adhesions is a procedure which has a considerable morbidity rate and thus another source of complications was introduced.

Ten years ago, A.P. treatment was still the subject of much discussion, although it was extensively employed. There was no general agreement on the results achieved and many of the published statistics were fallacious (Bloch, Tucker and Adams[1]). Also it had a bad reputation for complications, particularly among thoracic surgeons who so often had to deal with disasters following the use of A.P. in unsuitable cases. In fact the memory of these bad old days still lingers, or has been handed down as hearsay to those too young to remember, and thus it colours our attitude to A. P. treatment even today.

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In 1949 an investigation was started at the Brompton Hospital Sanatorium in an attempt to discover the prognosis of patients with cavitated disease treated by A.P., and also the effect of anatomically perfect or imperfect collapse on the prognosis. The results of this investigation were published in 1952 (Foster-Carter, Myers, Goddard, Young and Benjamin,[2] Foster-Carter[3]) by which time antibacterial treatment was firmly established and the indications for A. P. were getting fewer. Nevertheless, the findings still have considerable relevance and will be considered briefly. During the years 1937 to 1942, 442 patients were discharged from the Sanatorium with unilateral A. Ps. All these patients had cavitated disease and all were followed for a minimum of eight years, with an average of five years' observation after termination of

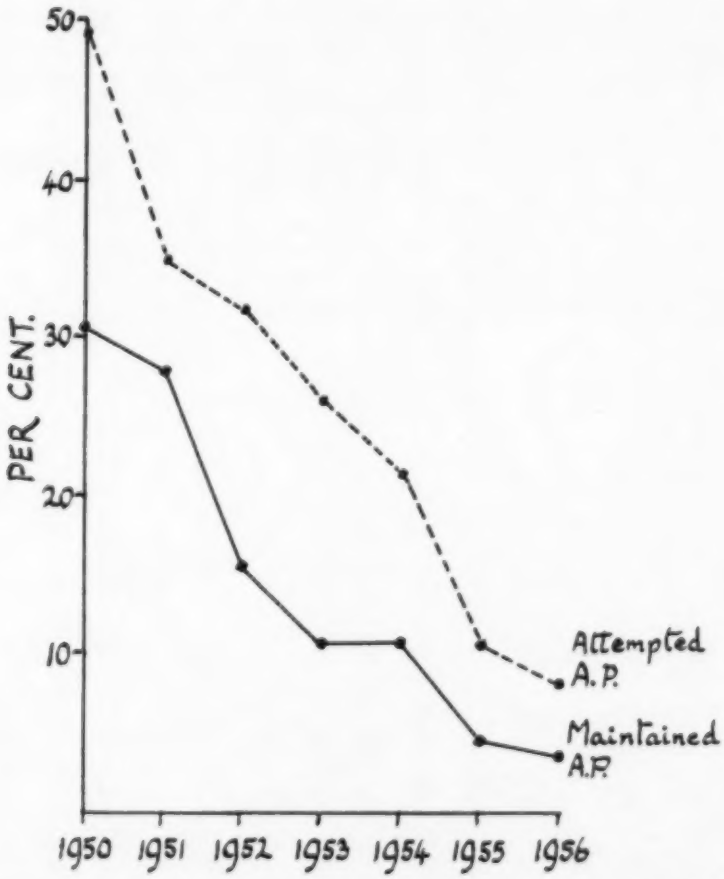

FIGURE 1: Graph showing the percentage of patients discharged from the Brompton Hospital Sanatorium during the past six years who had unilateral A. P. treatment. Continuous line: A. P. maintained. Dotted line: A. P. attempted (see Table I).

A.P. treatment; only just over 1 per cent were lost from observation. Some of the more important findings are shown graphically in Figure 3. The radiological grouping will be seen to correspond closely with the American National Tuberculosis Association classification and, since the initial extent of the disease is the most important single prognostic factor, great care was taken to see that groups were truly comparable in this respect. It will be seen that when cavity closure was achieved the results were good, regardless of the presence or absence of adhesions. In 230 patients with initial cavitation, most of whom had moderately advanced disease, the eight year survival rate was 90 per cent; a high figure considering that none of these patients had chemotherapy. When the A.P. failed to close the cavity the result was almost always bad;

TABLE I

PATIENTS DISCHARGED FROM BROMPTON HOSPITAL SANATORIUM 1950-1956: SHOWING FREQUENCY OF DIFFERENT FORMS OF TREATMENT

Year	1950		1951		1952		1953		1954		1955		1956	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Number of Patients	332	100	328	100	335	100	272	100	309	100	357	100	341	100
Number having Chemotherapy	165	50	243	75	291	87	254	94	305	99	357	100	341	100
Unilateral A. P.	102	31	96	28	58	17	31	11	38	12	14	4	11	3
Bilateral A. P.	14	4	15	5	2	0.6	3	1	1	0.3	....	....	....	....
Unsuccessful A. P.	46	28*	35	24*	46	43*	37	51*	30	44*	26	65*	16	59*
Total A. P. Attempted	162	49	116	35	106	32	71	26	69	22	40	11	27	8
Pneumoperitoneum	87	26	63	19	62	18	31	11	21	7	29	9	16	5
Resection	22	7	21	6	41	12	44	16	44	14	53	15	47	14
Thoracoplasty	36	11	21	6	40	12	32	12	25	8	31	9	18	5
Apicolysis with Plombage	12	4	11	3	25	7	28	10	18	6	19	5	6	2
No Active Treatment	59	18	101	31	107	32	103	38	162	52	211	59	243	71

*Per cent of all A. P's attempted.

of 113 such patients only 36 per cent survived eight years. The incidence of complications followed the same pattern; when cavity closure was obtained, the incidence of effusion was 25 per cent and of empyema 11 per cent; these figures were not affected by the presence or absence of adhesions. Of the patients who had persistent cavities no less than 36 per cent developed empyemas and half of these died.

Although none of the patients in this investigation had chemotherapy, the results are important for several reasons. They show that the bad reputation attached to A. P. in some quarters is due to poor selection of cases in the past and is undeserved; in fact, when used rightly, A. P. achieves remarkably good results. They show that cavity closure and not absence of adhesions is the key to successful A.P. treatment; adhesions which do not prevent cavity closure have no effect on the prognosis and do not increase the complication rate. Finally they provide a yardstick against which we can measure the achievements of the anti-

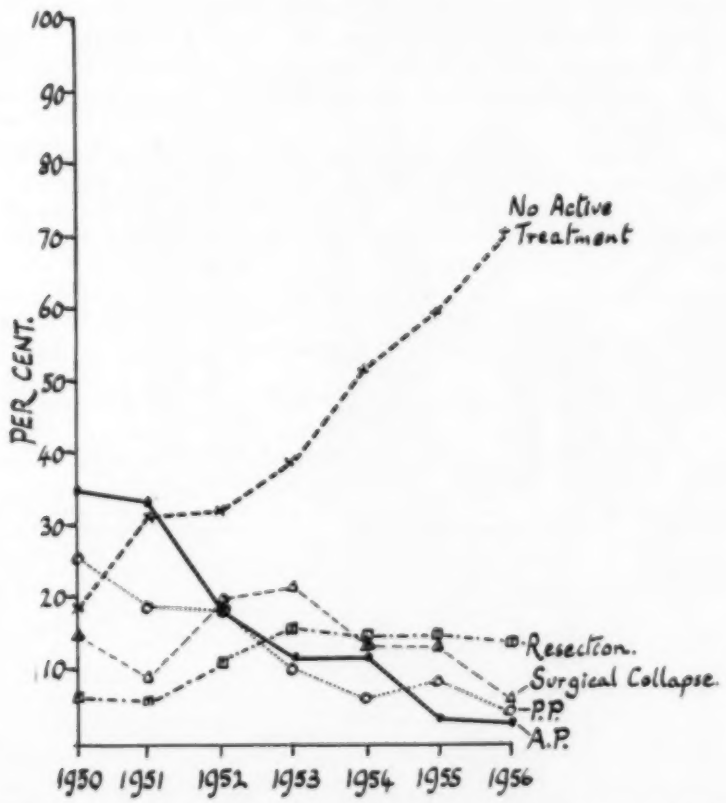

FIGURE 2: Graph showing the various forms of treatment undergone by patients discharged from the Brompton Hospital Sanatorium during the past six years (see Table I).

bacterial drugs in increasing the safety and efficiency of A.P. treatment today.

The Results of A.P. Treatment Combined with Chemotherapy

Evidence is steadily accumulating to show that modern chemotherapy has freed A.P. treatment from most of its former disadvantages (Birath,[4, 5] Scadding,[6] Dixon,[7] Thompson[8]). All authors agree that tuberculous empyema no longer occurs and that the incidence of pleurisy is reduced. This means that good functional results can be obtained in the vast majority of cases; Thompson[8] recorded marked pleural thickening in only 13 per cent of his patients while Birath[5] claims that if pleurisy is treated by rapid expansion of the lung, there is negligible loss of function in 95 per cent of cases.

Our own figures from the Brompton Hospital Sanatorium confirm these findings and suggest that still better results are being obtained as the duration of chemotherapy increases (Tables II and III). During the past six years there were discharged from this Sanatorium 174 patients who had been treated with chemotherapy and who also had established unilateral A. Ps. It will be seen from Table II that the duration of chemotherapy steadily increased throughout the series so that the later cases are not strictly comparable with the earlier ones. Quite apart from this, there are so many variable factors in pulmonary tuberculosis that any statistical assessment of the ultimate results of treatment would be unjustifiable on so small a series. Nevertheless all these patients have been followed up to the present time and their after-histories do enable us to decide whether the treatment achieved its immediate object and to assess the early complications.

Most commonly, A.P. was used to control cavitation and it succeeded in all cases. This was to be expected because it has become the practice to abandon any A.P. which is not producing cavity closure. Initial cavi-

TABLE II

TYPE AND DURATION OF CHEMOTHERAPY GIVEN DURING THE YEARS 1951-1956

Year	Type of Chemotherapy	Average Duration
1951	SM and PAS	3 Months
1952	SM and PAS	3 to 4 months
1953	SM and PAS Occasional INH	3 to 4 months
1954	SM, PAS and INH in various combinations	6 to 9 months Occasional long-term
1955	SM, PAS and INH in various combinations	9 to 12 months +
1956	SM, PAS and INH in various combinations	9 to 12 months +

tation was present in 122 patients, all had closed their cavities by the time of their discharge from Sanatorium and this was confirmed by tomography in most cases. In only four instances was there evidence of a cavity re-opening during the period of observation (Table III). Seventeen of the 174 patients relapsed (10 per cent), but most of these were treated in the earlier years when the duration of chemotherapy was short; in only eight was there evidence of fresh activity in the treated lung. There were two deaths, one following spontaneous pneumothorax in a patient who had an extensive contralateral thoracoplasty and one from gastric carcinoma. Apart from pleurisy, only seven patients had other complications; one was the spontaneous collapse already mentioned, the others were comparatively minor and comprised two other spontaneous pneumothoraces, a premature obliteration, and three

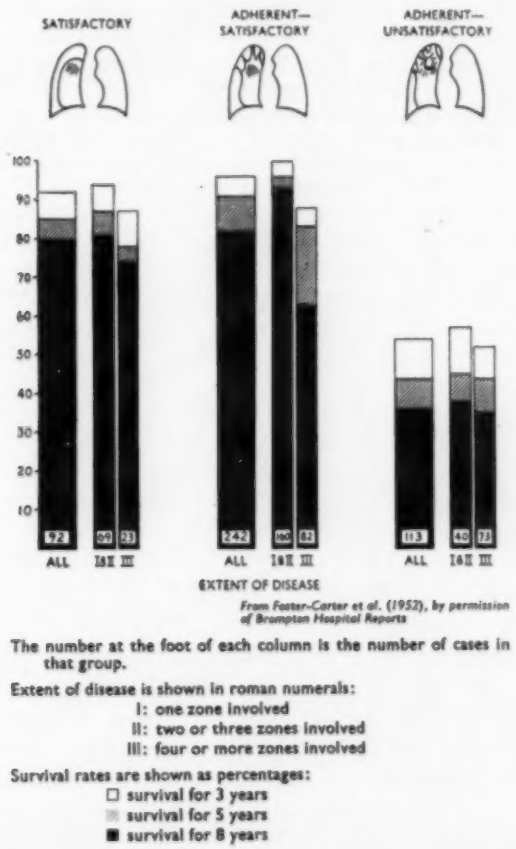

FIGURE 3: Survival of 442 unilateral A. P. cases before chemotherapy. *Satisfactory*—Free lung from start of A. P. or after adhesion section; cavities closed. *Adherent-Satisfactory*—Adhesions over diseased area which were not divided but cavities closed. *Adherent-Unsatisfactory*—Adhesions over diseased area but cavities did not close.

intrapleural haemorrhages only one of which was large enough to necessitate termination of the A.P.

No case of empyema occurred in this series but pleural effusion was still the most common complication; the total incidence was 17 per cent, which is much better than the 25 per cent found in our earlier series but is still of some consequence. Dixon[7] reported a similar incidence of effusion (20 per cent) in A.P. patients who had chemotherapy, whereas Thompson[8] and Birath[5] gave somewhat lower figures (11 per cent and 5 per cent respectively, although Birath's report only covered the first six months of treatment). Scadding[6] recorded only three transient, small effusions in 29 patients. The longer duration of chemotherapy in recent years has not been accompanied by a marked decrease in the number of effusions (Table III): Most of the patients who developed fluid did so in the first year and while still receiving antibacterial treatment. The effusions were usually small and transient; of the 174 A.P.s only 15

TABLE III

A. P. PATIENTS DISCHARGED FROM BROMPTON HOSPITAL SANATORIUM 1951-1956 WHO WERE TREATED WITH CHEMOTHERAPY

YEAR	1951	1952	1953	1954	1955	1956	TOTAL	
Minimum Follow-Up	5 Years	4 Years	3 Years	2 Years	1 Year	6 Months	Number	Per Cent
Number of A. P.'s	43	41	27	37	15	11	174	100
With Cavity	32	26	13	27	14	9	121	70
Sputum Culture + on Discharge	5	1	1	2	....	....	9	6
Cavity Opened Again Later	2	....	1	1	....	....	4	3
No Cavity	11	15	14	10	1	2	53	30
A. P. Terminated	40	30	24	33	4	....	131	75
Because of Effusion	3	4	3	3	2	....	15	9
A. P. Maintained	3	11	3	4	11	11	43	25
Relapsed	10	3	2	2	....	....	17	10
Effusion	7	9	5	6	3	....	30	17
Within One Year	6	6	3	4	3	....	22	13
After One Year	1	3	2	2	....	....	8	4
Other Complications	2	....	2	2	1	....	7	4
Died	1	1	....	....	....	....	2	1
Well at End of Follow-Up	41	39	25	35	14	11	165*	95

*Of the nine patients not known to be well at the end of the observation period, two had died; one had recently relapsed; six were well up to one year ago but final news not yet received.

(9 per cent) had to be terminated because of persistent fluid. It seems possible that while some effusions are due to tuberculosis, others may be the result of a foreign body reaction in the pleura; the former would be reduced by chemotherapy whereas the latter would not. It may be significant that Birath[4] reported an incidence of only 5 per cent of "spontaneous" effusions in his patients compared with 15 per cent in those who had adhesions divided.

In recent years there has been a growing tendency to terminate without undue delay any A.P. which is not achieving its object. Table I shows that in 1950 only 28 per cent of all A.Ps. attempted were rejected as unsatisfactory, while in 1956 that figure had more than doubled. Because of this careful selection the functional results are now excellent and, as Thompson[8] has pointed out, they compare favourably with those following resection. Even a tendentious comparison made by Fleming[10] between old A.P. patients who had no chemotherapy and a series of carefully prepared resection patients, all of whom received antibacterial drugs, failed to show more than a slight difference in function between the two groups.

The Present Position

In view of the excellent results of modern A.P. treatment it may well be asked why the use of the method has declined to the extent shown in Figure 1. The most important reason is that the majority of the patients who would have been regarded as ideal subjects for A.P. treatment five years ago, now recover with antibacterial treatment and rest alone. A clear indication of the paramount position being achieved by chemotherapy will be seen in Table I (Figure 2), which shows that the percentage of patients receiving no "active" treatment has increased from 18 per cent in 1950 to 71 per cent in 1956. This increase has been at the expense of all other forms of treatment, but particularly A. P. and pneumoperitoneum. The latter procedures were used mainly to control small localised lesions with minimal cavitation and these are just the lesions which respond well to chemotherapy. More severe lung damage still requires surgical intervention, but the number of operations is not increasing and will probably decline as the antibacterial drugs are used for longer periods.

Contemporary Indications for A.P. Treatment

We may safely assume that in future all patients will have at least three months' initial treatment with antibacterial drugs, after which candidates for A.P. treatment will be selected from the relatively small number whose response to chemotherapy is not satisfactory. With this proviso, the main indications for A.P. treatment are:

1. Localised disease with cavitation.
2. Localised cavitation with widespread disease throughout the lung.
3. Localised cavitation in one lung when there is serious disease requiring surgical collapse in the other.

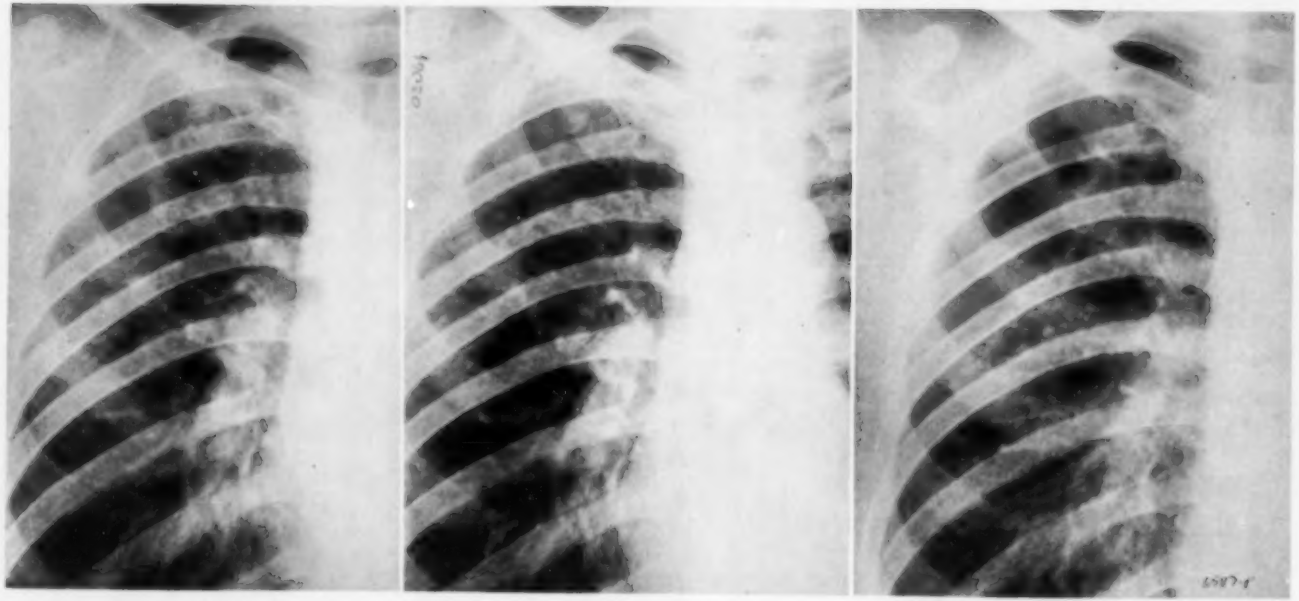

FIGURE 4 FIGURE 5 FIGURE 6

Figure 4: Man aged 29. Infiltration and a cavity in right in upper lobe.—*Figure 5:* Same patient after three and one-half months' chemotherapy. Cavity smaller but persisting.—*Figure 6:* Same patient after right A. P. Apical adhesions but cavity closed.

4. Localised cavitation in one lung when the other has virtually been put out of action by extensive surgery.

It is assumed that in all cases the cavitation is persisting and has ceased to improve, in spite of adequate chemotherapy.

Localised disease with cavitation is, in our experience, by far the most common indication for A.P. treatment at the present time. The situation in which it arises can best be illustrated by a short protocol:

G. C. Man, aged 29. A Veterinary Surgeon. Admitted to hospital in January 1956; sputum positive for tubercle bacilli; early tuberculous laryngitis; x-ray film showed infiltration and a cavity in the right upper lobe (Figure 4). May 1956, after three and one-half months' rest with daily streptomycin, INH and PAS: cavity smaller but still present and showing no sign of further diminution (Figure 5). Right A.P. induced; a few apical adhesions present but cavity closed and sputum converted within a month (Figure 6). September 1956, returned to full work. May 1957, still having chemotherapy; tomographs confirm cavity closure and resolution of lesions; A.P. treatment to be terminated.

In order to realise the advantages of A. P. treatment in such a case as this, let us consider the alternatives:

First: Continuation of antibacterial therapy alone. This may well succeed in the end, but it often takes many months. In the case under consideration the patient, who was a junior partner in a busy practice, was most anxious to get back to his work. He could not have been permitted to do so while he still had a cavity and positive sputum. No other form of treatment would have enabled him to return to work in so short a time.

Second: Resection. This is a major operation with an appreciable morbidity and a small mortality. Not infrequently the surgeon finds that he has to remove more of the lung than was originally estimated and this may necessitate a small thoracoplasty in addition. A.P., in contrast, is essentially a temporary and reversible procedure which leaves the lung

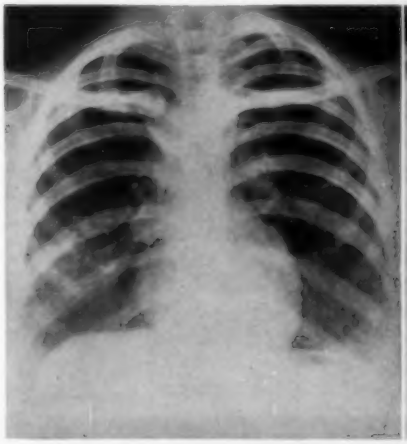

FIGURE 7

FIGURE 8

Figure 7: Woman aged 22. After three months' chemotherapy. Extensive infiltration right middle and lower lobes with a persistent cavity in middle lobe. Patient anxious to avoid operation.—*Figure 8:* Same patient two months later after right A. P.

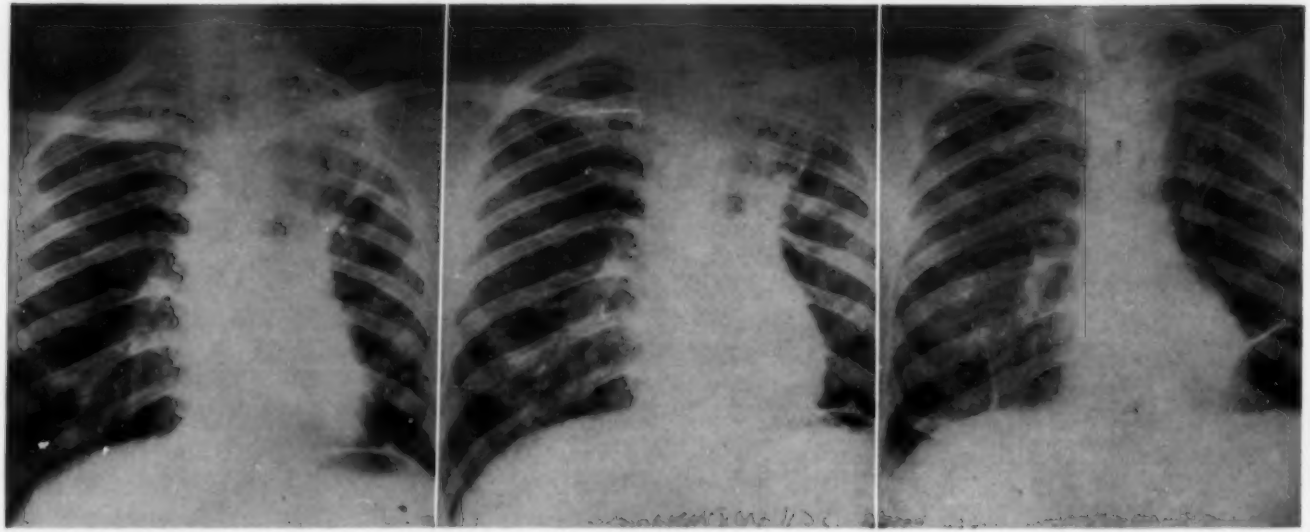

FIGURE 9 FIGURE 10 FIGURE 11

Figure 9: Man aged 33. After six months' chemotherapy. Sputum positive. Infiltration right upper lobe with cavity. Collapse and consolidation with cavitation left upper lobe and infiltration with small cavity in apex of left lower lobe.—*Figure 10:* same patient after right A. P. Apical adhesions but cavity closed.—*Figure 11:* Same patient after left upper lobectomy. Sputum negative. Disease in left lower lobe healing.

intact and should give a functional result equal, and often superior to, that following resection. There is nothing to be lost in attempting pneumothorax because if it is not satisfactory a resection can still be performed. Another less important but very practical advantage of A.P. treatment is that it avoids the ugly scar of a surgical operation; a benefit much appreciated by young women.

Third: Pneumoperitoneum. The pulmonary relaxation obtained by this method is limited, unless it is accompanied by temporary phrenic interruption, and there is a growing disinclination to use this combination because of the danger of permanent diaphragmatic paralysis. The concentric relaxation obtained by a satisfactory A.P. is much more effective than that produced by a pneumoperitoneum alone. The latter still has a limited use in the treatment of patients with widespread disease who are not responding to chemotherapy and who are unsuitable for A.P. treatment or surgery.

Having examined the alternatives it will be seen that there is much to be said for trying A.P. treatment when one wishes to control a limited, cavitated lesion. A trial pneumothorax can do no harm; if it does not achieve its object it can be terminated without delay and little time will have been lost. If however it does control the disease satisfactorily, a good result may confidently be expected, the patient's return to work is accelerated, and a major surgical operation may well have been avoided.

The second indication—localised cavitation with widespread disease throughout the lung—is an extension of the first, but surgical treatment is no longer an easy alternative. Resection of the cavitated area is frequently followed by re-activation of one or more of the residual lesions: surgical collapse therapy may control apical cavitation but it cannot be used if the cavity is in the lower part of the lung (Figure 7). It seems rational to try A.P. treatment in these circumstances, because it not only promotes cavity closure but also relaxes the whole lung and thus assists the healing of the diffuse lesions, instead of subjecting them to added strain. A.P. has also been shown to be particularly successful in the treatment of cavities in the apex of the lower lobe (Crofton[11]).

The remaining two indications for A.P. treatment are much less commonly seen but deserve mention. The use of an A.P. to control localised cavitation in one lung before embarking on surgical measures to deal with more extensive disease in the other, will sometimes avoid the need for bilateral surgery (Figures 9 to 11). The temporary and reversible character of pneumothorax renders it particularly suitable in this situation where surgical treatment for both lungs might leave the patient a respiratory cripple. This applies also to the final indication; the use of A.P. to control a fresh, small cavitated lesion in the "good" lung of a patient who has lost the function of the other lung after extensive surgery. Here again a successful A.P. will control the disease without eventual loss of respiratory function when the pneumothorax is terminated (Figures 12 and 13). The great danger associated with A.P. when the function of the contralateral lung is grossly impaired is the occurrence of spon-

taneous pneumothorax. This complication is uncommon if the A.P. is skilfully managed, but the one death in our series was due to this cause. When confronted with a case of this type, the clinician has to weigh the possible risks of A.P. against the probable result of surgery and the decision may be difficult.

Contra-indications and Management

The contra-indications to A.P. treatment are still very much the same as they were before the advent of chemotherapy. It is essentially a temporary measure and should not be used if there is extensive lung destruction. Care should be taken to ensure that the patient is not suffering from tuberculous bronchial ulceration; signs of bronchitis or the presence of atelectatic areas or tension cavities usually contra-indicate A.P. treatment. Lastly, A. P. will not affect large solid tuberculous foci in the lung.

Having induced A.P., the success or failure of the treatment will be judged solely by its effect on cavitation. If cavity closure is not achieved within a reasonable time—say one month— the A.P. should be terminated. If however cavity closure does occur, then any adhesions which are presented may safely be left alone. In our opinion cauterisation of adhesions ought now to be abandoned. It is an operation which inevitably damages the pleura and is often followed by a troublesome effusion which is unlikely to respond to chemotherapy. Also the diminished use of A.P. is bound to reduce the number of surgeons having the necessary experience to undertake this operation, the success of which has always de-

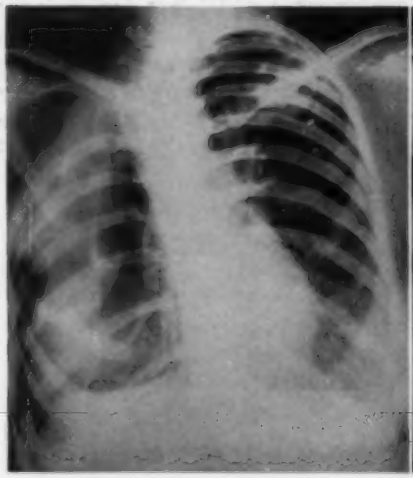

FIGURE 12

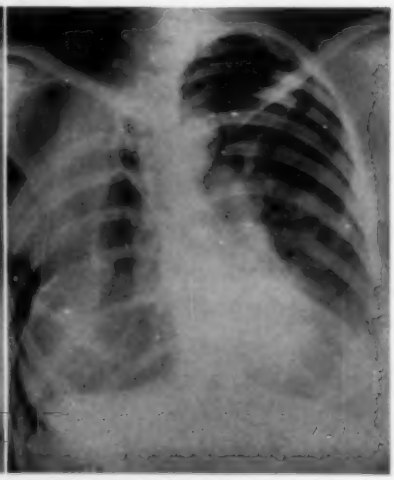

FIGURE 13

Figure 12: Woman aged 32. Right lung immobilised by old thoracoplasty followed by upper lobectomy and post-operative empyema. Cavity in left upper lobe. Sputum positive; unaffected by prolonged chemotherapy (Resistant to SM, INH and PAS).—*Figure 13:* Same patient after left A. P. Numerous apical adhesions but cavity closed and sputum negative.

pended so largely upon the skill of the operator. Therefore when adhesions are preventing cavity closure, it is probably best to abandon the A.P. forthwith in favour of some alternative method of treatment.

The condition of the pleura must be watched carefully if good function is to be preserved. Small effusions are harmless provided that the fluid does not rise above the diaphragm and that it absorbs in a few weeks. Large or persistent effusions demand energetic treatment, because they so often lead to pleural thickening and impairment of function. Rapid expansion of the lung is always indicated and may be achieved by the technique which Birath[9] has described. This includes postural treatment with the patient lying on the sound side, abdominal breathing exercises, and frequent pleural aspirations. We have not found the introduction of antibiotics into the pleural cavity to be advantageous or desirable.

The maintenance of A.P. also requires skill and experience and the best results are obtained when the patient is able to remain under the care of the same physician for the whole duration of the treatment (Young[12]). Formerly about three years was considered the best length of time to maintain an A.P., although slight disease was often treated for shorter periods. There is no doubt that the time can now be drastically reduced and 12 to 18 months is known to have been sufficient in many cases. It is highly probable that, with long-term chemotherapy, an even shorter duration of collapse would give satisfactory results. Before the days of antibacterial drugs it was not uncommon to see cavity closure achieved by an A.P. which was regarded as unsatisfactory and terminated after only a few weeks' duration. Cavities which close during antibacterial treatment seldom re-open and it now seems reasonable to try the effect of allowing the lung to expand quite soon after the A.P. has achieved its object. A great advance will have been made if it proves possible to obtain permanent cavity closure by means of pneumothorax which need be maintained only for the period of hospital treatment.

Conclusion

In conclusion it may be said that antimicrobial drugs have now assumed such a paramount position in tuberculosis therapy that all other forms of treatment, both medical and surgical, have become merely ancillary. Nevertheless artificial pneumothorax still has a small but important part to play in the treatment of patients whose response to chemotherapy is not entirely satisfactory, and short-term pneumothorax may well prove to be increasingly useful in promoting the rapid closure of cavities.

SUMMARY

Analysis of 174 patients, treated with unilateral pneumothorax and chemotherapy during the past six years, suggests that most of the former disadvantages of artificial pneumothorax have now disappeared; but it is also shown that more effective chemotherapy is reducing the need for artificial pneumothorax, in common with other forms of treatment.

Artificial pneumothorax still has a small but important role in treat-

ment; reasons are given why it is preferable to other types of therapy in certain situations.

It is suggested that the practice of cauterisation of adhesions is no longer necessary and should now be discontinued.

The duration of artificial pneumothorax can now be greatly reduced and the use of this treatment for short periods may prove to be valuable in promoting quick cavity closure.

RESUMEN

Un análisis de 174 enfermos tratados con neumotórax unilateral durante los últimos seis años, sugiere que la mayoría de las desventajas antes achacadas al neumotórax artificial ahora han desaparecido; pero también se ha mostrado que la quimioterapia más efectiva ahora, ha reducido la necesidad del neumotórax, así como otras formas de tratamiento.

El neumotórax tiene aún un papel pequeño pero importante en el tratamiento; se dan las razones de por qué es preferible a otros tipos de tratamiento en ciertas condiciones.

Se sugiere que la práctica de la cauterización de adherencias ya no es necesaria y ahora debe abandonarse.

La duración del neumotórax artificial puede ahora reducirse grandemente y el uso de este tratamiento por corto tiempo, puede ser valioso para producir el cierre pronto de las cavernas.

RESUME

L'étude de 174 malades, traités par pneumothorax unilatéral et chimiothérapie pendant les six années passées, suggère que la plupart des inconvénients anciens du pneumothorax artificiel ont maintenant disparu; mais elle montre également que la chimiothérapie plus efficace est en voie de réduire la nécessité du pneumothorax artificiel ainsi que d'autres formes de traitement.

Le pneumothorax artificiel a encore un rôle, petit mais important dans le traitement. L'auteur donne les raisons pour lesquelles il est préférable à d'autres types de traitement dans certaines situations.

L'auteur suggère que la pratique de cautérisation des adhérences n'est plus nécessaire et devrait être abandonnée.

La durée du pneumothorax artificiel peut maintenant être beaucoup réduite et l'emploi de ce traitement pour de petites périodes de temps peut être tenu pour valable car il permet la fermeture rapide des cavernes.

ZUSAMMENFASSUNG

Die Analyse von 174 Patienten, die während der verflossenen 6 Jahre mit einseitigem Pneumothorax und Chemotherapie behandelt wurden, legt die Vermutung nahe, dass die meisten der früheren Nachteile des künstlichen Pneumothorax heute nicht mehr bestehen; es ist aber auch gezeigt worden, dass eine besser wirksame Chemotherapie die Notwendigkeit eines künstlichen Pneumothorax herabsetzt, ebenso wie auch anderer Behandlungsformen.

Der künstliche Pneumothorax besitzt noch eine geringe, aber wichtige

Bedeutung bei der Behandlung; es werden Gründe dafür angeführt, weshalb er in gewissen Situationen anderen Behandlungsarten vorzuziehen ist.

Es wird angenommen, dass die Praxis der Durchtrennung von Verwachsungen nicht länger erforderlich ist und jetzt aufgegeben werden sollte.

Die Dauer des künstlichen Pneumothorax kann jetzt auch beträchtlich verringert werden, und die Benutzung dieser Behandlung für kurze Zeit kann sich als wertvoll erweisen für die Begünstigung eines raschen Kavernenverschlusses.

Acknowledgments: My thanks are due to the Medical Committee of the Brompton Hospital, London, for permission to publish the statistics here recorded. I am also much indebted to Miss K. Colegate for her work on the follow-up and to Mr. D. Kemp for the x-ray reproductions.

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Coexistence of Fungi and Tubercle Bacilli*

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The presence of fungi in the sputa of newly admitted patients in a tuberculosis hospital has been investigated in order to determine the coexistence of fungi and tubercle bacilli in the lungs of patients with pulmonary tuberculosis. Larkin and Phillips[1] have reviewed the literature on coexistent pulmonary tuberculosis and fungal disease. These authors reported three cases of dual fungal-tuberculosis infection with a poor prognosis. Greer and Gemoets[2] have suggested a symbiotic relationship between tubercle bacilli and coexisting fungi. They noticed a tendency for pulmonary tuberculosis to develop a more devastating course when it is associated with an invasion of parasitic fungi. Mankiewicz[3] demonstrated a stimulating effect of Candida albicans on the growth of Mycobacterium tuberculosis, in vitro. Though the pathogenicity of this fungus is questionable, its occurrence in the sputum of patients with pulmonary tuberculosis is of general interest.

The media used for isolation of fungi were blood agar containing 40 micrograms penicillin G and 40 micrograms of streptomycin per ml.; Littman's oxgall agar containing 30 micrograms streptomycin per ml., and Sabouraud's glucose agar containing 40 micrograms of penicillin and 40 micrograms of streptomycin per ml. Blood agar supported growth in all isolations of Histoplasma capsulatum; Littman's medium did not support growth in any case while Sabouraud's medium supported growth in 50 per cent of the isolations of H. capsulatum.

All newly admitted patients were studied for a period of 11 months. Three separate sputum specimens were collected from each of 505 patients.

Tables I and II demonstrate the result of this investigation.

As indicated in Table IV, during this study four cases of unsuspected histoplasmosis were diagnosed. M. tuberculosis was not cultured from any one of these patients. Cryptococcus neoformans and Geotrichum candidum were coexistent with M. tuberculosis in one patient each. These findings suggest the advisability of frequent sputum cultures for fungi in a tuberculosis hospital.

Mankiewicz[3] studied the possible effect of Candida albicans on the growth of M. tuberculosis since the two organisms were frequently isolated from the same sputum. At this hospital the patient's response to therapy in cases of dual infection with Candida albicans and Mycobacterium tuberculosis is being investigated.

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**Presently at Mountain Home, Tennessee.

TABLE I
PATIENTS WITH SPUTA POSITIVE OR NEGATIVE FOR FUNGI

	Total	Per Cent
Total number of patients	505	100
With negative fungus cultures	277	54.8
With positive fungus cultures	211	41.8
With contaminated fungus cultures	17	3.4

TABLE II
INCIDENCE OF TYPES OF FUNGI

	Total	Per Cent
Total patients positive for fungus	211	100
Positive for Candida species	205	97.1
Positive for Cryptococcus neoformans	1	0.5
Positive for Geotrichum candidum	1	0.5
Positive for Histoplasma capsulatum	4	1.9

Yeast-like fungi were isolated in 40.6 per cent of the patients. Table III shows the incidence of positive and negative cultures for fungi and tubercle bacilli.

TABLE III
INCIDENCE OF POSITIVE AND NEGATIVE CULTURES FOR FUNGI AND TUBERCLE BACILLI

	Total	Per Cent
Total number of patients (except those with all cultures contaminated)	487	100
Negative for tubercle bacilli and fungi	85	17.5
Negative for tubercle bacilli, positive for fungi	74	15.2
Positive for tubercle bacilli and fungi	137	28.1
Positive for tubercle bacilli, negative for fungi	191	39.2

TABLE IV
INCIDENCE OF POSITIVE CULTURES FOR FUNGI ACCORDING TO SPECIES

Cultures Positive for Fungi	Culture for M. Tuberculosis	
	Negative	Positive
Candida albicans	57	100
Candida sp.	13	35
Cryptococcus neoformans	0	1
Geotrichum candidum	0	1
Histoplasma capsulatum	4	0

SUMMARY

The sputa of all newly admitted patients were cultured for fungi during a period of 11 months. Four cases of histoplasmosis were detected among 505 patients. M. tuberculosis was not cultured from any one of these. However, Cryptococcus neoformans and Geotrichum candidum were co-existent with M. tuberculosis in one patient each.

RESUMEN

Durante once meses se cultivaron los esputos de todos los enfermos ingresados buscando hongos en ellos. Se descubieron cuatro casos de histoplasmosis entre 505 enfermos. En ninguno de estos se cultivó la micobacteria tuberculosa. Sin embargo, el criptococcus neoformans y el geotricum candidum coexistieron con la micobacteria tuberculosa en un caso.

RESUME

Les expectorations de tous les malades nouvellement admis furent mises en cultures pour la recherche d'éléments mycosiques pendant une période de onze mois. Quatre cas d'histoplasmose furent découverts sur 505 malades. Dans aucun de ces cas le bacille tuberculeux ne fut décelé par culture. Cependant, des malades ont été observés chez qui coexistaient avec le bacille de Koch chez l'un le cryptococcus neoformans, chez l'autre le geotrichum candidum.

ZUSAMMENFASSUNG

Der Auswurf neu aufgenommener Patienten wurde während eines Zeitabschnittes von 11 Monaten kulturell auf Pilze verarbeitet. Es wurden 4 Fälle von Histoplasmose gefunden unter 505 Kranken. Bei keinem von diesen liess sich M.-tuberculosis kulturell gewinnen. Jedoch kamen Cryptococcus neoformans und Geothrichum candidum gleichzeitig mit M.-tuberculosis bei je einem Patienten vor.

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SECTION ON CARDIOVASCULAR DISEASES

The Correction of Mitral Insufficiency With a Trans-Valvular Polyvinyl Formalinized Plastic (Ivalon) Sponge Prosthesis*

A Preliminary Report

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During the past half century a tremendous amount of work has been done in developing surgical methods to control mitral insufficiency. The pathological changes found in this disease, the disturbed physiology and the basic principles involved in the various corrective measures which have been used, have been well discussed in previous writings.[1-16] As a result of this work many phases of the problem are reasonably well understood and agreed upon. Experience has shown that the introduction of prostheses in general has produced rather discouraging results for a number of reasons. The same can be said for methods involving sutures placed near the edges of the opposing mitral leaflets. On the other hand, suture methods which bring about leaflet apposition by altering the contour or the size of the annulus fibrosus have produced definitely encouraging results.[8 14 15] In spite of this, the overall progress which has been made to date in solving the problem has not been sufficiently great as to dispel further attempts to develop better methods. The purpose of this communication is to give a preliminary report on a technique involving the introduction of a trans-valvular prosthesis which embodies certain established principles plus additional factors which seem to simplify the technical problem of correcting mitral insufficiency and may provide lasting beneficial results.

Background for Method

The introduction of foreign material or even autogenous tissues into the region of the mitral valve has been associated with a high incidence of early and late complications, some of which are poorly understood. Thrombi are prone to form on exposed sutures or irregular surfaces of most intracardiac foreign substances and may cause serious or fatal arterial embolization.[11 16 17] A hemorrhagic tendency not infrequently develops with diffuse oozing from all cut surfaces. This bleeding usually fails to respond to standard therapeutic measures. The cause of this state is not clear but

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seems to be most troublesome when moveable foreign material is placed into the blood stream, especially if the mass comes into repeated contact with adjacent tissues causing trauma to the cellular elements of the blood.[5, 18] In addition to these complications, hemolysis of greater or lesser severity develops in a significant number of cases and is associated with the usual clinical and laboratory findings present when excessive erythrocyte destruction is present. Although careful studies have been reported recently[19] the overall problem is not well understood. The magnitude of these three complications alone has been sufficiently great so as to strongly deter the general clinical use of most types of prostheses.

In experimental animals the rarity of these complications, particularly those of thrombo-embolic nature when polyvinyl formalinized plastic sponge (Ivalon) prostheses were placed across the left ventricle between the mitral leaflets[7] or across the mitral valve from atrium to ventricle[13] immediately begs for an explanation. A likely one is that this plastic material becomes much like living tissue very soon after its introduction into the blood stream, due to the ingrowth of vascular fibrous tissue into the interstices of the sponge followed by the formation of a smooth, glistening surface covering which grossly and microscopically is indistinguishable from the adjacent endocardial tissue.[7, 13, 20, 21] Most solid substances preclude such changes because of their inherent physical properties and even living autogenous or homogenous tissue transplants are apt to show early changes of non-viability with the inflammatory and thrombotic complications associated with this state. Implanted sponge has been shown to produce minimal inflammatory and necrotic changes in living tissue adjacent to it and only mild thickening of the valvular endocardium which comes in contact with it during valve closure.[7, 13] In addition, it appears to maintain its size and much of its pliability in contrast to autogenous or homogenous tissues which generally swell, then shrink to a fraction of their original size.[7, 10] In experimental animals intracardiac implantation has not been followed by complicating infections.[7, 13] Regardless as to what theoretical or practical explanation is given, Ivalon seems to be well tolerated experimentally and also clinically by patients receiving intracardiac patches or aortic grafts. The rarity of complications seemed to justify further use of this material, particularly when its physical properties make it a very usable and adaptable substance in dealing with the technical problems involved in repairing an insufficient mitral valve. Its texture is soft so that a rough form made before the time of surgery can be shaped and trimmed readily at the operating table to fit the defect found between the mitral leaflets, regardless of its size and shape. This soft texture seems to allow it to become compressed and molded by the opposing cusps so as to fit the exact contour of their firm, irregular edges. Its workable characteristics make it possible to fashion a prosthesis as a single piece with extensions through which anchoring sutures may pass and thus expose to the blood stream nothing but the Ivalon itself. Although this softness and pliability has definite advantages, it was soon learned during experiments on dogs, post-mortem hearts and dead beef hearts, that in

order to stop the flow of fluid under approximately 120 mm. of mercury pressure through a defect it was necessary to have the size of the Ivalon approximately 25 per cent greater than the opening. Also, it was soon learned that such excessive bulk was objectionable because the mass of Ivalon above the line of cusp contact would tend to "bulge over" and thus obstruct the flow of blood from the atrium into the ventricle. Further experimentation using a simple type of pulse duplicator demonstrated that the insertion of a solid rod into the center of the soft Ivalon would maintain the peripheral pliability and moldability and still produce obstruction of a defect with a prosthesis of only slightly greater size (Fig. 1). This principal was applied clinically by placing a compressed Ivalon insert of appropriate size and shape into a slit in the body of the prosthesis.

Preparation of Prosthesis

The prosthesis is carved from a block of Ivalon about 2 x 4 x 18 cm. in size, using a sharp, long-bladed knife and scissors. It is cut so that it consists of 3 anchoring tails and a wedge-shaped body approximately 2 x 4 x 4 cm. in dimensions with the greatest cross section or base toward the ventricular chamber. In the early cases the base of the wedge was placed in the atrium with the apex in the ventricle. Later, however, the wedge was inverted in order to minimize the tendency to inflow obstruction (Fig. 2, A, B, C,). Two anchoring tails extend proximally from the apex or atrial aspect of the wedge and a single tail from the center of the base. Heavy No. 2 braided silk is then threaded through each atrial tail passing through the corresponding side of the body and out the ventricular tail. It is important to fix the heavy silk securely to the encasing Ivalon tails using two or three interrupted fine silk sutures to prevent the tails from tele-

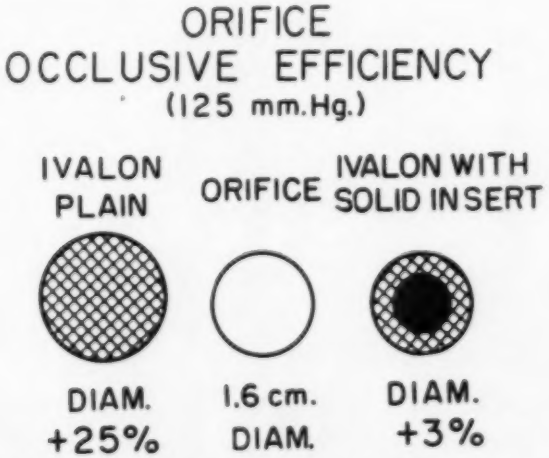
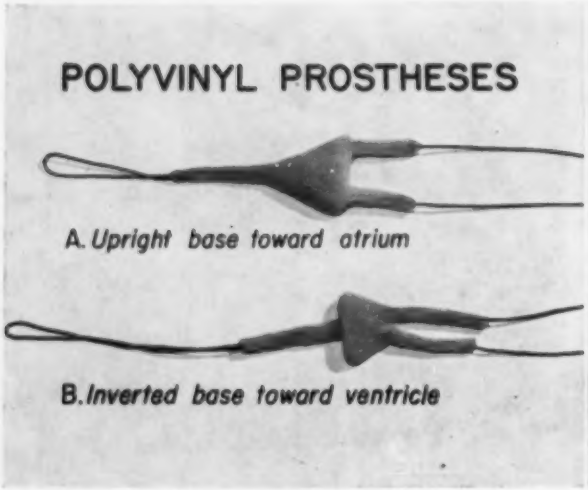
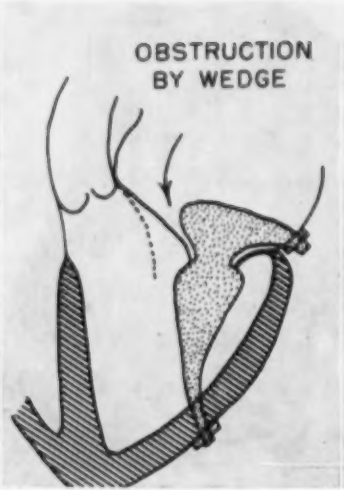


FIGURE 1: The flow of water under 125 mm. of mercury pressure through a circular valvular defect 1.6 cm. in diameter can be stopped by an Ivalon column of 25 per cent greater diameter. Using a solid rod insert one-half of the linear diameter of the Ivalon column, the same occlusive effect is obtained with an overall diameter increase of only 3 per cent.





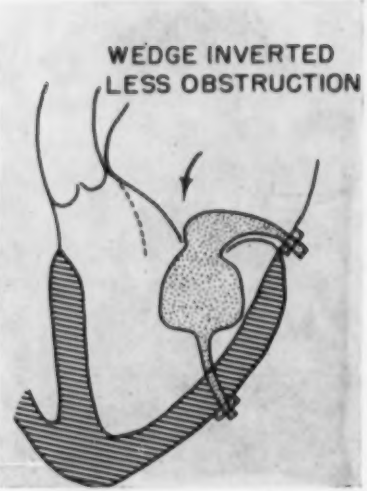


FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2A: A) Model of original upright prosthesis with base of wedge toward atrium. B) Current model with apex and two anchoring tails toward atrium. Anchoring silk shown passing through prosthesis.—*Figure 2B:* Base of plain Ivalon wedge toward atrium showing tendency of soft Ivalon to "bulge" over line of closure producing ventricular inflow obstruction. *Figure 2C:* Wedge inverted to minimize obstruction.

scoping or bunching up on the heavy silk as the anchoring tails are pulled out through the walls of the heart. The tails should be about 5 mm. in diameter, which is large enough to tamponade the puncture wounds in the heart muscle and thus control bleeding. The roughly formed prosthesis is then washed well, preferably overnight in running water in a screened vessel. It is then autoclaved under water along with the instruments to be used for the case or it can be sterilized by boiling for 20 minutes. The compressed Ivalon, which is to be used for the firm insert, is prepared by packing long rods of well washed sponge into a glass test tube until it is reduced to approximately ¼ of its original volume, after which it is sterilized as above. After removal from the tube it will be found to be about the consistency of medium soft latex rubber. At the operating table the defect in the valve is examined and an appropriately shaped fragment of the compressed Ivalon, approximately ½ the linear dimensions of the body, is inserted into a slit in the prosthesis after which it is closed with fine buried sutures (Fig. 3). The prosthesis is then finally trimmed to a shape as near that of the orifice as possible and to a size 5 to 10 per cent larger than the insufficient opening. It is then soaked with penicillin solution and is ready for insertion.

Introduction of the Prosthesis

The heart is exposed through a long, routine posterolateral incision below the 6th rib, which is cut posteriorly (also 5th, if necessary). An umbilical tape is placed around the aorta just distal to the subclavian artery and passed through a broad based flexible tourniquet which will allow aortic compression during any manipulation which grossly obstructs the flow of blood across the mitral valve. We feel that this is important since it aids greatly in maintaining adequate central aortic, coronary and cerebral arterial pressure which otherwise would drop to dangerously low

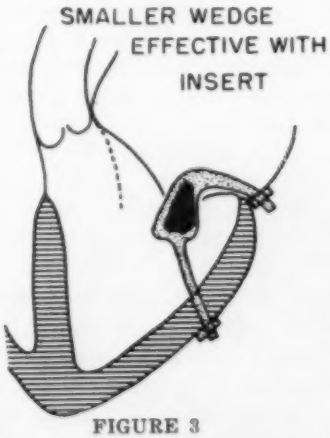


FIGURE 3

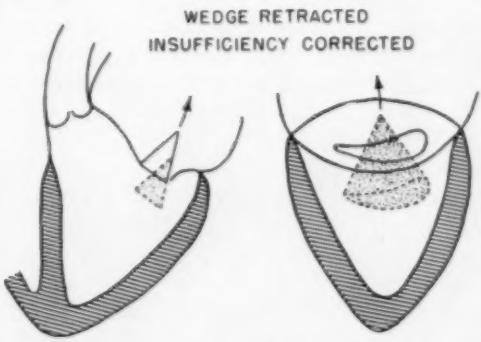


FIGURE 4

Figure 3: Insert of compressed Ivalon approximately 50 per cent of linear diameter of wedge increases occlusive efficiency and allows for decreased overall size of prosthesis.—*Figure 4:* Diagram showing adjustability of prosthesis after insertion into the heart by advancement or retraction.

levels.[22] The pericardium is incised posterior to the phrenic nerve to expose the entire lateral surface of the heart, including the atrioventricular junction to the region of the termination of the coronary sinus. Heavy silk sutures are placed in the pericardium to allow strong traction which rotates the heart outward to provide adequate exposure. A purse string suture is placed around the base of the auricular appendage, using closely placed stitches to minimize the likelihood of tearing out which might result from repeated manipulations through the atrial incision and the ends controlled with a flexible tourniquet. The atrium and the valve are then explored, paying particular attention to the flexibility of the major leaflet, since if adequate mobility is not present or cannot be attained through generous commissurotomy, both anterolaterally and posteromedially, then the lesion probably is not amenable to correction by the use of any fixed or relatively fixed prosthesis. To obstruct such a defect in the absence of good mobility of the major leaflet would simply convert insufficiency into stenosis. One can be more liberal with the commissurotomy using whatever technique is necessary, inasmuch as the prosthesis can be shaped to correct any increased leakage, particularly if it occurs toward the mural leaflet. Even if some disruption of the chordae tendineae of this cusp occurs, the prosthesis is apt to correct it, since mechanically it functions somewhat like a large chordal structure if the atrial tail is placed in the region of the chordal damage. Appropriate sites of exit for the ventricular and atrial tails are then chosen to center the prosthesis opposite the point of maximal leakage. The site in the ventricle should be approximately ½ the distance from the apex to the atrioventricular junction and as far away from the major coronary branches as possible. The atrial exit points are chosen just proximal to the vessels in the atrioventricular junction and should be situated so that the angle made by the two tails is very near a straight line. It is important to place the posterior tail very far back—farther than one would anticipate—and near the termination of the coronary sinus, so that the wedge can be pulled into the posteromedial commissure where the maximal leak is apt to be present. A malleable suture passer with an eye in its distal end is then threaded with the heavy anchoring silk emerging from the ventricular tail, and this is passed through the atrium along the ungloved right index finger down into the ventricular chamber, using care not to entangle the papillary muscle or chordae tendineae, and out the chosen ventricular site. (An alternative method is to pass the instrument in a retrograde fashion, thread it and pull it back out the ventricular wall.) Traction on the ventricular tail then advances the body of the wedge into the atrium, with or without removing the finger, and downward into the ventricle. Great care must be used to pull in the proper axis in order to avoid tearing the friable ventricular muscle. Bleeding from the ventricular wound is usually controlled by the bulk of the tail, although a round button of Ivalon is usually pulled over it and against the surface of the myocardium. The process is repeated with each atrial tail, using extreme care to pull in the proper axis to avoid laceration of the thin atrial wall. However, if this should occur, hemorrhage can be

controlled readily by placing the intra-atrial finger against the tear while sutures are placed externally. The position of the body of the prosthesis is then adjusted by advancement or retraction to increase or decrease the cross sectional area of the wedge lying between the leaflets (Fig. 4). The two atrial tails are then adjusted to pull the wedge toward one commissure or the other in order to bring about maximal obliteration of the regurgitant jet. After the best possible control is attained the tails and the buttons are sutured to the myocardium using several stitches, after which the redundant ends of the tails are excised. It is important to use care in placing these sutures, since the ventricular contractions postoperatively may have a tendency to slide the buttons away from the ventricle with resultant hemorrhage, especially after pericardial roughening has occurred. The chest cavity is then irrigated well with saline solution and closed in a routine manner.

Results

I. Tolerance of Operation:

Dogs tolerated the technical procedure of introducing the prostheses very well, and rather surprisingly, the five patients—four of whom were Class IV patients with low reserves—had virtually no more difficulty with hypotension, arrhythmias or other problems than one would expect from a simple commissurotomy in such patients. Obviously, blood loss was somewhat greater than for a simpler procedure but with adequate replacement no difficulty was encountered. The tolerance of our first patient was particularly notable, since she was very close to the state of uncontrollable decompensation with massive ascites and hydrothorax, which responded very slowly to preoperative medical management (Fig. 5). On two occasions her surgery had to be cancelled because of the development of tachycardia with a rate of around 180 followed by pulmonary congestion. In spite of this, she was scheduled a third time and went through the procedure with no significant difficulty, other than a spell of tachycardia lasting for about 2 minutes before responding to neostigmine.

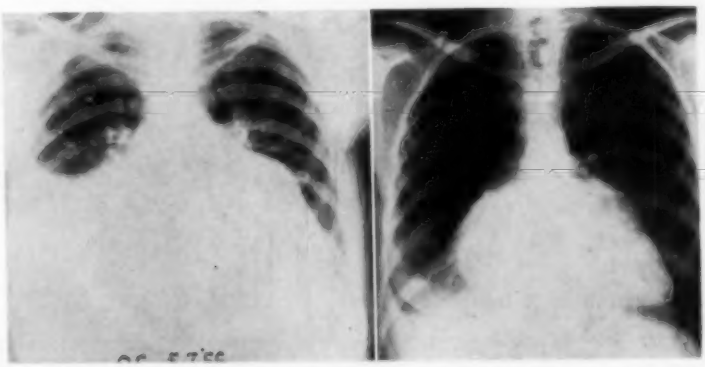


FIGURE 5: Chest roentgenograms showing type of Class IV patient selected for surgery before and after intensive medical preparation.

II. Degree of Correction:

In animals attempts were made to estimate the efficiency of the prostheses in correcting regurgitation produced by biting out a semicircular piece of the mural cusp. However, after several experiments we became convinced that the pathology of such insufficiency was not comparable to that found in patients and, therefore, the effectiveness of the method could not be judged. Further experiments to settle this point were therefore abandoned. Our initial plan, to quantitate the degree of correction of insuffciency, was to take simultaneous left ventricular and left atrial pressures before and after repair, in addition to estimating the volume by palpation, which admittedly is a gross determination. However, in animal experiments as well as clinical cases, the pressure measurements added significantly to the operative time and also gave unexpected conflicting results which led to efforts to explain them. On one occasion, when by palpation, the volume of the residual jet seemed to be small, the intra-atrial pressure, as recorded, was found to be unexpectedly high. We therefore set up a simple experiment measuring the pressures in a fluid-filled container into which a circular jet of water was flowing at a pressure corresponding to approximately 120 mm. of mercury. Using a beveled needle to control the position accurately, great variation in pressure readings was found depending on the relationship of the needle tip to the jet and also on the relationship of the bevel to the jet (Fig. 6).

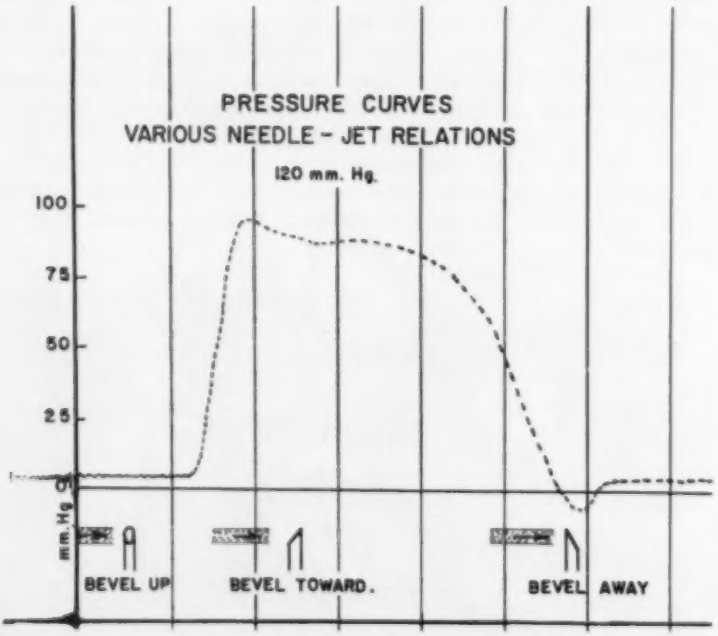


FIGURE 6: Chart showing marked variation in pressures in a chamber depending on the relationship of needle tip to the entering jet of fluid.

The pressures varied from a maximum of near 100 mm. of mercury to a negative reading of approximately minus 4 mm. of mercury. This wide variation, which was brought about by only one of the many variables, i.e., rotation of the needle bevel, caused us to doubt the validity of such pressure readings until other factors are better controlled. In 3 patients it was estimated that approximately 80 per cent of the regurgitant jet had been obliterated and 75 per cent in a fourth, even though simple, uncompressed Ivalon was used. In the fifth patient approximately 85 per cent correction was attained using a smaller prosthesis containing a compressed insert. In two instances, the prosthesis definitely was not pulled sufficiently far into the posteromedial commissure, so that considerable leakage persisted in this area (Fig. 7). Definite evidence of stenosis has not developed in any case to date, although in one instance we are concerned about this possibility. Here a prosthesis was used in the face of a relatively small orifice and somewhat questionable leaflet mobility after the cross-polar plication method failed when the internal suture pulled out. A mitral stenotic murmur is present, but as yet no objective or subjective evidence of stenosis has appeared.

III. Hemorrhagic Diathesis:

Fortunately, an outspoken picture of a true hemorrhagic state has not been encountered, as yet. One patient died postoperatively primarily from hemorrhage, although the site, most likely, was the ventricular wound which was unusually large due to technical difficulties in pulling the prosthesis through the wall. This patient had a congenital absence of the pericardium which, throughout the years, allowed her progressively enlarging heart to shift backward into the posterior gutter. In the absence of the pericardial sac there was nothing which could be grasped

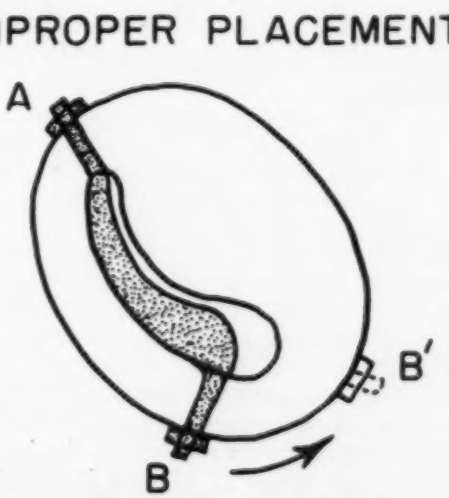


FIGURE 7: Prosthesis improperly placed being centered too far anteriorly, thus allowing persistent posterior leak. Shift of exit point of atrial tail, B to B^1, would correct this difficulty.

safely in order to rotate the heart around into a position of adequate surgical accessibility. The bleeding, which was evident before closure, seemed to be very well controlled but sutures were not placed around the periphery of the Ivalon button, due to the proximity of the descending branch of the left coronary artery. It seems likely that motion postoperatively caused recurrence of the bleeding, and this impression was substantiated by the escape of fluid from this tract when the ventricle was distended post-mortem. Platelet counts, clot retraction, bleeding and clotting time determinations have not been notably altered in the postoperative period.

IV. Hemolytic Reaction:

The development of anemia with an increase in serum bilirubin, after the effects of bleeding related to surgery were passed, occurred in one patient to a moderate degree, thus requiring four 500 cc. blood transfusions during the first five days after operation. A second patient, who died postoperatively, developed definite evidence of hemolysis of considerable degree along with an unexplainable hyperpnea up to 70 per minute immediately on awakening from the anesthetic and persisting for 48 hours. Check-up examination on the transfused blood excluded a hemolytic transfusion reaction beyond reasonable doubt. The discovery at autopsy of pigment gall stones and splenomegaly in this 18 year old youth suggested a pre-existing hemolytic defect, although all pre- and postoperative studies failed to establish its nature. Three survivors up to 5 months postoperatively have not become anemic. How important hemolysis may prove to be cannot be stated in view of our present knowledge.

V. Thrombo-embolic Phenomena:

To date, signs or symptoms suggesting thrombo-embolic complications have not been recognized.

VI. Other Complications:

No evidence of postoperative infection or of other significant complications has been encountered.

Discussion

The technical maneuvers involved in the method described appear to be tolerated relatively well, even in patients who have advanced heart disease with a low cardiac reserve. Correction of mitral insufficiency by taking advantage of the principle of progressive advancement of a wedge-shaped prosthesis through the mitral orifice seems to be simpler technically and more controllable than most other methods. The prosthesis described, which has adequate firmness due to the insertion of a centrally placed fragment of compressed Ivalon plus peripheral soft moldability, appears to possess physical properties inherently capable of obliterating mitral insufficiency to a greater degree than is possible with other materials due to its ability to conform to the irregular, firm, cusp edges. The extremely low incidence of thrombo-embolic phenomena in animals and the absence of such complications in the few patients treated to date is encouraging, but by no means excludes the possibility of such

complications. The frequency and seriousness of hemorrhagic and hemolytic reactions cannot be estimated at the present time. Neither can the possibility of late stenosis be excluded. Because of these considerations, the indiscriminate and widespread application of this method is certainly not advisable until some of the above questions are answered by further observations and further passage of time.

SUMMARY AND CONCLUSIONS

1. A method for correcting mitral insufficiency using a transvalvular polyvinyl formalinized (Ivalon) sponge has been described.

2. Experience with placement of Ivalon in the region of the mitral valve in experimental animals and in a few patients indicates that the incidence of serious complications is low. This may well be due to the ingrowth of vascular fibrous tissue and surface "endothelialization." The characteristics of the implanted Ivalon become somewhat similar to living tissue.

3. The technique, as described, appears to be well tolerated and the degree of correction of the insufficiency can be controlled within reason after the prosthesis has been placed within the heart.

4. Experience with the method is so limited that the operative mortality rate, the incidence of complications and the results cannot be estimated at the present time.

5. The early results seem to be favorable enough to justify further limited clinical application but widespread clinical use is inadvisable.

RESUMEN Y CONCLUSIONES

1. Se describe un método para corregir la insuficiencia mitral usando una esponja transvalvular de polivinilo formalizado (Ivalon).

2. La experiencia con la colocación del Ivalón en la región de la válvula mitral en los animales de experiencia en algunos enfermos indica que la incidencia de complicaciones serias, es baja. Esto bien puede deberse a la penetración de tejido vascular fibroso neoformado y en la creación de una superficie de "endoepitelización."

Las características del Ivalón implantado se hacen algo similares al tejido vivo.

3. La técnica como de describe, parece conducir a una buena tolerancia y el grado de corección de la insuficiencia puede controlarse razonablemente después de que prótesis se ha colocado en el interior del corazón.

4. La experiencia en el método es tan limitada que la mortalidad operatoria, la incidencia de las complicaciones y los resultados no pueden estimarse aún al presente.

5. Los resultados tempranos parecen suficientemente favorables para justificar su empleo ulterior en aplicación clínica limitada pero el uso extenso clínicamente no es aconsejable.

RESUME

1. L'auteur décrit un procédé pour corriger l'insuffisance mitrale, en utilisant une éponge transvalvulaire en polyvinyle formolée (Ivalon).

2. L'expérience avec la mise en place de l'éponge d'Ivalon dans la région de la valvule mitrale chez les animaux et chez un petit nombre de malades montre que la fréquence des complications graves est faible. Ceci pourrait bien être dû à l'accroissement de tissu vasculaire fibreux et à une "endothélialisation" de surface. Les caractères de l'Ivalon greffé deviennent en quelque sorte semblables à ceux du tissu vivant.

3. La technique, selon la description qui en a été donnée, semble être bien tolérée, et le degré de la correction de l'insuffisance peut être contrôlé rationellement après que la prothèse a été placée dans le coeur.

4. L'expérience de cette méthode est encore si limitée que le taux de mortalité opératoire, la fréquence des complications, et les résultats ne peuvent être estimés pour le moment.

5. Les résultats précoces semblent être suffisamment favorables pour justifier des essais cliniques ultérieurs limités, mais l'emploi étendu en pathologie médicale ne doit pas encore être conseillé.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNG

1. Es wurde eine Methode beschrieben zur Korrektur der Mitralinsuffizienz unter Verwendung eines mit Formalin (Ivalon) behandelten transvalvulären Polyvinylschwammes.

2. Erfahrungen mit der Unterbringung von Ivalon in der Gegend der Mitralklappe bei Versuchstieren und bei einigen wenigen Patienten ergibt, dass das Auftreten von ernsthaften Komplikationen selten ist. Dies kann sehr wohl die Folge sein des Einwachsens von gefässhaltigem Bindegewebe und einer oberflächlichen "Endothelialisierung." Die Eigenschaften des implantierten Ivalons werden bis uz einem gewissen Grade denen des lebenden Gewebes ähnlich.

3. Die Technik, wie sie beschrieben wird, scheint gut vertragen zu werden, und das Ausmass der Korrektur der Insuffizienz kann bis zu einem gewissen Grade beherscht werden, nachdem die Prothese im Herzen angebracht ist.

4. Die Erfahrung mit dieser Methode ist so begrenzt, dass die operative Sterblichkeit, die Häufigkeit von Komplikationen und die Ergebnisse im Augenblick noch nicht abgeschätzt werden können.

5. Die Anfangserfolge scheinen günstig genug zu sein, um in begrenztem Rahmen weitere klinische Anwendung zu rechtfertigen, jedoch ist allgemeine Benutzung nicht ratsam.

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The Occurrence of Arrhythmias in Acute Myocardial Infarctions

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Introduction

Numerous statistical studies have been made on arrhythmias occurring in persons with acute myocardial infarctions. Most investigations have been made and reported from teaching hospitals in large medical centers. For this reason such studies have usually been carried out on patients of a similar social and economic status, not necessarily a true cross section of the general population. We believe it worthwhile to undertake a similar type of study of all patients treated for acute myocardial infarctions who were seen in two community general hospitals during a five year period (1950-1954). Thus our report attempts to evaluate such studies made on a group representative of all economic and social spheres.

Method of Study

Only those with clinical evidence of acute myocardial infarction such as pain, fever, leukocytosis, and elevated sedimentation rate were included in this study. All of them had definite electrocardiographic evidence of acute infarctions. A total of 187 patients was selected as fulfilling these criteria. They were studied from a standpoint of occurrence as arrhythmias in relation to location of the infarction, hypertension, sex, age, and mortality and other complicating factors, such as cardiac failure and shock.

Findings

Incidence, Age, and Sex: The percentage of arrhythmias occurring, excluding extrasystoles and bundle branch block, was 16.5 per cent (31 of 187 cases). This value compares with those of Mintz and Katz[1] who found 16.4 per cent in a study of 572 cases. Master et al[2] found 14 per cent in a review of 300 cases. Totibouet[3] in France found 8 per cent in a study of 420 cases while Griffith[4] reported an incidence of 17 per cent in myocardial infarction from the Los Angeles County Hospital.

There was an increased incidence of arrhythmias in the older age groups. Among the group of patients with arrhythmias there were 24 (77.4 per cent) over 60 years of age and 7 (22.6 per cent) under 60 years. In all cases of infarctions there were 111 (59.4 per cent) over 60 years of age and 76 (40.6 per cent) of 187 patients under 60 years of age. There was not only an increased incidence of arrhythmias but also an increased mortality in the older age groups. Twenty of 26 deaths with anterior infarction were in patients over 70 years of age and 10 of 18 deaths with posterior infarctions were in those over 70 years old (Table I).

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From the total number of cases studied, there were 89 (47.3 per cent) with an anterior and 98 (52.7 per cent) with a posterior infarction. Although the total incidence of anterior and posterior infarctions was nearly the same, the sex incidence was considerable different. Men constituted 75.9 per cent of all cases studied and women 24.1 per cent. The men had an incidence of 63 (70.5 per cent) of the 89 cases of anterior infarction while the women had 26 (29.5 per cent). Of those with posterior infarction 79 (80.6 per cent) were in men and 19 (19.4 per cent) were in women. This would suggest that a proportionately higher incidence of posterior infarction occurred in men. In this series 81 per cent of the arrhythmias occurred in men and 19 per cent in women. This is nearly the same proportion as infarction occurred in the two sexes, indicating that the arrhythmias appeared with similar frequency in both sexes. Master[2] reported that arrhythmias were more prone to develop in women than in men while Mintz and Katz[1] stated that the incidence was about the same in both sexes. In our series of arrhythmias there was an incidence of 10 cases (10.6 per cent) with anterior infarction and 21 (22.4 per cent) with posterior infarction (Table I, II and III).

Types of Arrhythmias: The most common type of arrhythmias was auricular fibrillation. It occurred in 16 (8.7 per cent) of a total of 187 patients. There was an incidence of 8 (9.1 per cent) of 89 with anterior infarction and 8 (8.2 per cent) of 98 with posterior infarction.

TABLE I

AGE DISTRIBUTION OF ALL CASES WITH MYOCARDIAL INFARCTION

Age in Years	Number of Cases
31 - 40	4
41 - 50	18
51 - 60	54
61 - 70	61
71 - 80	43
81 - 90	7
TOTAL	187

AGE DISTRIBUTION OF CASES WITH ARRHYTHMIAS

Age in Years	Number of Cases
41 - 50	3
51 - 60	4
61 - 70	12
71 - 80	10
81 - 88	2
TOTAL	31

Atrioventricular block was noted in 11 (5.9 per cent). Of these, only one occurred with anterior infarction. This case was associated with a first degree block. Ten (10.1 per cent) of 98 patients with posterior infarction had heart block, in seven of whom it was complete. Because the right coronary artery supplies the atrioventricular node in 92 per cent of patients,[5] nearly all cases of atrioventricular block are associated with posterior artery occlusions.

Ventricular tachycardia was recorded in only one instance and this was a patient with posterior infarction. He also developed a nodal tachycardia during his stay in the hospital.

One case of auricular flutter was noted. In various series in the literature the incidence of flutter has been reported from 1 per cent to 4.3 per cent. Master[2] reported 1 per cent in 300 cases and Mintz and Katz[1] found 4.3 per cent in 524 patients with acute myocardial infarctions.

There was no case of auricular tachycardia identified in our series, however, there were two with nodal rhythms. These types of arrhythmias have been reported to be uncommonly associated with acute myocardial infarctions. Bellet[6] stated that supraventricular tachycardia was seen in only 5 of 1,247 cases of myocardial infarctions. In a series of 872 patients reviewed by Askey[7] only eight had supraventricular tachycardia.

Complicating Factors: Hypertension (blood pressure over 160/90) was found in 56 (29.9 per cent) of the patients. Of these there was an incidence of 31.9 per cent with an anterior infarction and 29 per cent with posterior infarction. Another complicating factor, appearing with almost equal frequency in both anterior and posterior infarction, was shock, with a total incidence of 14.5 per cent. There was 13.5 per cent in anterior infarction and 15.5 per cent in posterior infarction. Heart failure occurred in 29 (15.5 per cent). Of those with heart failure 18 (20.2 per cent) were in the group with anterior infarction and 11 (11.2 per cent) in the posterior infarctions cases (Table IV).

Mortality: The over-all mortality was 23.5 per cent in 187 patients. The mortality of those with arrhythmias was 29 per cent (9 of 31 cases) while the rate in those without arrhythmias was 22.4 per cent (35 of 156 cases). The rate in all patients with anterior infarctions was 29.2 per cent and in posterior infarction it was 18.3 per cent. There was a mortality of 20.3 per cent among the men and 33.3 per cent among the women. Anterior infarction caused deaths more frequently in men than did posterior—26.8 per cent to 15.6 per cent, respectively. Mortality was essen-

TABLE II
PERCENTAGE OF PATIENTS WITH ANTERIOR AND POSTERIOR MYOCARDIAL INFARCTION

	Anterior	Posterior	Total
Males	70.5	80.6	75.9
Females	29.5	19.4	24.1

tially the same in women with either anterior or posterior infarctions—34.5 per cent to 31.5 per cent. Patients having heart failure and myocardial infarction had a higher mortality (49 per cent). In those in whom shock occurred, mortality was 52 per cent, and in those with auricular fibrillation it was 31 per cent. Two of the seven with complete heart block died (Table V).

Discussion

Arrhythmias in acute myocardial infarction are known to increase the mortality. Rosenbaum and Levine[9] found the mortality to be increased from 27 per cent for those without arrhythmias to 42 per cent for those with arrhythmias. Our mortality for 31 with arrhythmias was 29 per cent compared to 22.4 per cent in cases without arrhythmias. These findings seem to be in agreement with others.[2, 10] Hence it would appear that the prompt and accurate diagnosis and treatment of arrhythmias in myocardial infarction might be life-saving.

Auricular fibrillation was the most common arrhythmia in our series. This type had a mortality rate of 31 per cent which was greater than our over-all mortality of 23.5 per cent. Rosenbaum and Levine[9] thought the occurrence of auricular fibrillation after myocardial infarction did not appreciably alter the prognosis. Any increase in mortality has been ascribed to heart failure or shock rather than to the arrhythmia. However, Askey[11] felt the prognosis was worse if the arrhythmia persisted. Also he stated that the longer the fibrillation persisted, the greater became the hazard of embolism. Billings[12] found that the presence of auricular fibrillation at the time of the acute attack increased the mortality during the first 30 days.

A high incidence of auricular fibrillation has been reported to be associated with lateral wall infarction by Wood, Wolferth and Bellet.[13] Cushing[14] found a high incidence in solitary atrial infarctions. He observed abnormalities of the auricular mechanism of the electrocardiogram in 74 per cent of the cases of atrial infarction. Others[1, 9, 12] noted no correlation between auricular fibrillation and the location of the infarct. In our series

TABLE III

PERCENTAGE OF VARIOUS ARRHYTHMIAS OCCURRING IN ANTERIOR AND POSTERIOR INFARCTION

	Anterior	Posterior	Total
Arrhythmias—Excluding extrasystoles and B.B.B.	10.6	22.4	16.5
Auricular Fibrillation	9.1	8.2	8.7
Atrioventricular Block	1.1	10.1	5.9
Ventricular Tachycardia	0	1.0	0.5
Nodal Tachycardia	0	2.0	1.4
Auricular Flutter	0	1.0	0.54

there was an equal number of patients with anterior and posterior infarctions who were found to have auricular fibrillation.

Heart block is another type of arrhythmia commonly associated with myocardial infarctions. Goldman[15] stated that it is generally agreed that complete heart block following myocardial infarction is practically always associated with posterior infarction. Fifty-nine of 60 cases of heart block reported by Master[16] had posterior infarctions. All of our cases of complete heart block were associated with posterior infarctions. As previously noted, the one case occurring with anterior infarction had first degree block. Gross[5] pointed out that the blood supply to the auriculoventricular node is usually from the right coronary artery and this is the likely reason of heart block being associated with posterior infarction. Master[16] stated that the atrioventricular node is very sensitive to ischemia, so any cause of anoxia can produce heart block.

Mortality is distinctly higher when heart block occurs. Mintz and Katz[1] reported 100 per cent, but Bellet[6] found recoveries were not so rare. In our series two of seven cases with complete heart block, one of first degree block, and the one with sino-auricular block died. Rosenbaum and Levine[9] reported that once heart block develops in association with acute myocardial infarction, and the patient survives, complete recovery from the block or a lesser degree of block tends to be the ultimate outcome. Graybiel and White[17] found 10 per cent of patients with complete heart block had had myocardial infarctions.

In our series other types of arrhythmias were uncommon. Only one case of auricular flutter and one of ventricular tachycardia were noted. However, these types could have occurred more commonly than were diagnosed. This might have been true in terminal states where rapid cardiac rates were noted either in the physicians' or nurses' notes but were not further identified.

Ventricular tachycardia occurs most often in association with organic heart disease.[18] Cooke and White[19] in reviewing the records of 25,000 patients at Massachusetts General Hospital found 27 instances of ventricular tachycardia. Twenty-two of these had coronary heart disease. They further state that considering the large number seen with coronary heart disease, there were few instances of ventricular tachycardia and that coronary heart disease by itself must play only a minor role in initiating this arrhythmia. Infarction with its various disturbances in the muscle and circulation should provide numerous occasions for the escape of the ectopic

TABLE IV

PERCENTAGE OF COMPLICATIONS OF MYOCARDIAL INFARCTION

	Anterior	Posterior	Total
Hypertension	31.9	29.0	29.9
Shock	13.5	15.5	14.5
Heart Failure	20.2	11.2	15.5

rhythmic centers; however, the incidence is extremely small. Digitalis has been known to precipitate ventricular tachycardia as have other substances.[18,20] Only two of Cooke and White's 22 patients with ventricular tachycardia survived longer than two years after the attack.

Ambrust and Levine[20] reviewed 107 cases of ventricular tachycardia and found that 79 (74 per cent) had coronary heart disease. Forty-four of the 79 had myocardial infarctions. The duration of the attacks may be a few seconds to days—one having been reported to have lasted 71 days.[20] Sixty-four of the 79 cases reported by Ambrust and Levine were dead within one month.

Supraventricular tachycardias are much more frequently associated with non-organic heart disease.[18] Master,[3] however, reported five supraventricular tachycardia out of 300 cases of myocardial infarctions. Only one of the 300 had ventricular tachycardia. Mintz and Katz[1] reported an incidence of 3.2 per cent of supraventricular tachycardias in their patients with myocardial infarctions while 5.3 per cent had ventricular tachycardias. Supraventricular tachycardias are usually not serious except in the presence of myocardial infarction and then they may be fatal unless quickly stopped. Sinus tachycardias rarely exceed a rate of 140 but the persistence of such a rapid rate with myocardial infarctions carries a poor prognosis. Billings et al.[12] noted that mortality in myocardial infarction was much higher in those with pulse rate over 100.

Arrhythmias were more common in those with posterior infarctions in our series. The incidence was 22.4 per cent compared to 10.6 per cent in anterior infarctions. Mortality was higher in those occurring with anterior infarctions which may have been due to the fact that the percentage with heart failure was twice as high in anterior as in posterior infarction. Mortality in those with heart failure was 55 per cent with anterior infarctions and 45 per cent with those with posterior lesions.

TABLE V

PERCENTAGE OF MORTALITY FROM ANTERIOR AND POSTERIOR INFARCTION AND COMPARISON WITH ASSOCIATED COMPLICATING FACTORS AND SEX RELATIONSHIP

	Anterior	Posterior	Total
Deaths—with Heart Failure	55.0	45.5	49.0
Deaths—with Shock	58.0	53.0	52.0
Deaths—with Auricular Fibrillation	12.5	50.0	31.0
Deaths—with Heart Block	100.0	30.0	36.5
Deaths—Males	26.8	15.6	20.3
Deaths—Females	34.5	31.5	33.3
Mortality of all Cases	29.2	18.3	23.5

The exact mechanisms of arrhythmias remain unknown. However, the two factors principally involved in auricular fibrillation are increased parasympathetic stimulation of the vagus and anoxia of the myocardium. Of these factors anoxia would seem the more important in myocardial infarctions. Schlichter[21] observed the development of auricular fibrillation in a case of anemia and its disappearance after blood transfusion. According to Luisada[22] the most common cause of infarction is slow, gradual occlusion of an arteriosclerotic vessel by the concentric proliferation of the intima. Anoxia of the myocardium is the result. The common association of atrial infarction[14] with supraventricular arrhythmias would only serve to support the theory that anoxia is a likely etiologic factor. Since arrhythmias usually do not begin until several hours after infarction, Harris[23] believed that possible sympatho-adrenal substances liberated during necrosis of the muscle act as excitatory factors on the vagus to produce auricular fibrillation.

The treatment of these arrhythmias has been well covered in the literature. The cases studied were attended by various staff members of the two hospitals in which our study was made. Hence no attempt is made to evaluate the treatment in this study.

We feel that the dangers of the use of digitalis in patients with acute myocardial infarctions have been overemphasized. We agree with Askey[24] that quinidine should be given with digitalis, especially when premature beats appear. The fear of the production of ventricular tachycardia has deterred many physicians from using digitalis in acute infarctions when complicated by heart failure or auricular fibrillation. Gilson and Schemm[25] administered digitalis to patients with heart failure and ventricular tachycardia and found that the tachycardia disappeared and the heart failure was controlled. The authors believe that both digitalis and quinidine are contraindicated in the presence of complete heart block.

SUMMARY

1. Arrhythmias, excluding extrasystoles and bundle branch block, were found to be present in 16.5 per cent (31 of 187 cases) of acute myocardial infarctions reviewed in a study from two community general hospitals.

2. The over-all mortality of acute myocardial infarctions was 23.5 per cent and was higher among those with other complicating factors, such as heart failure or shock. Mortality of the patients with arrhythmias was 29.2 per cent (9 of 31) while the mortality in patients without arrhythmias was 22.4 per cent.

3. The relationship of the incidence of various types of arrhythmias to sex, age, site of infarctions and other complicating factors, such as heart failure and shock, has been discussed.

RESUMEN

1. En 16.5 por ciento de los infartos agudos del miocardio, se encontraron arritmias, excluyendo extrasístoles y bloqueo de ramas, según un estudio realizado en dos hospitales generales públicos.

2. La mortalidad global de los infartos agudos del miocardio fué 23.5 por ciento y fué más alta entre los que tenían otros factores complicantes tales como insuficiencia cardiaca o schock. La mortalidad entre los enfermos con arritmias fué 29.2 por ciento (nueve entre 21) en tanto que la mortalidad en enfermos sin arritmias fué de 22.4 por ciento.

3. Se ha discutido la relación de la incidencia de varios tipos de arritmias al sexo, edad, sitio del infarto y otros factores complicantes tales como insuficiencia cardiaca y schock.

RESUME

1. Mis à part les extrasystoles et le bloc de branches, l'auteur a constaté des arythmies dans 16,5% des cas (31 sur 187) d'infarctus aigus du myocarde, recueillis dans deux hôpitaux généraux publics.

2. La mortalité moyenne des infarctus aigus du myocarde a été de 23,5% et se montra plus élevée chez les malades atteints de complications, telles qu'insuffisance cardiaque ou shock. La mortalité des malades atteints d'arythmies fut de 29,2% tandis que la mortalité des malades sans arythmies fut de 22,4%.

3. L'auteur a discuté les rapports entre les différents types d'arythmies et le sexe, l'âge, le siège de l'infarctus et les autres facteurs de complications, tels que l'insuffisance cardiaque et le shock.

ZUSAMMENFASSUNG

1. Arrhythmien ausser Extrasystolen und Herzblock wurden vorgefunden in 16,5% (31 von 187 Fällen) von akutem Myocard-Infarkt, die in einer Untersuchungsreihe aus 2 städtischen allgemeinen Krankenhäusern einer Durchsicht unterzogen wurden.

2. Die Gesamtsterblichkeit des akuten Myocard-Infarktes betrug 23,5% und lag höher bei solchen mit anderen komplizierenden Faktoren wie Herzinsuffizienz oder Schock. Die Sterblichkeit der Patienten mit Arrhythmie betrug 29,2% (§ von 31) während die Mortalität bei Patienten ohne Arrhythmie bei 22,4% lag.

3. Besprechung der Beziehungen des Vorkommens verschiedener Typen von Arrhythmien zu Geschlecht, Alter, Lage eds Infarktes und anderen komplizierenden Faktoren so wie Herzinsuffizienzbund Schock.

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CURRENT THERAPY

The Editorial Board invites your comment.

Rest in Myocardial Infarction*

It is generally agreed that rest is a mandatory adjunct in the treatment of acute myocardial infarction. Any injured body tissue is known to heal more rapidly if the part is kept at rest, and since the injured myocardium must obviously continue to work while it is healing, it seems only rational to keep the work load as light as possible by the avoidance of any activity which would call for an increased cardiac output. There are a few physicians who treat patients with acute infarctions on an ambulatory basis; however, we feel that this procedure definitely entails an increased risk to the patient, to say nothing of the increased risk to the doctor if the patient's family is at all inclined toward malpractice suits. The main points of contention in regard to rest in this disease involve the questions, where, how, and how long.

It is our policy to hospitalize all cases of established or "impending" myocardial infarction for a period at least long enough to permit thorough evaluation. Hospitalization facilitates closer observation of the patient which renders easier the classification into "good risk" or "poor risk." It is much easier to obtain the desired laboratory work including electrocardiograms in the hospital, adequate treatment is more readily obtained, and any complication is likely to be detected much earlier. Some physicians have advanced the argument that it is dangerous to move a patient with an acute infarct to a hospital, particularly if shock is present, but we maintain that the presence of shock is an additional strong reason for getting the patient into the hospital as quickly as possible. This statement is made on the assumption that adequate ambulance service is available, including attendants to carry the patient, and oxygen equipment. It is seldom, if ever, necessary for the ambulance to rush to the hospital at full speed with siren screaming; most urban patients live within a few miles of a hospital, and the few minutes saved by rushing do not compensate for the increased discomfort to the patient. In the case of the rural population, it is probably true that very long ambulance trips should be avoided even if the patient must be treated in the home. This is becoming less of a problem, however, as more hospitals are being constructed in the smaller communities.

If a patient is established as a good risk case, he may be treated in the home after one or two weeks in the hospital, but if he is considered a bad risk or if any complication develops, he is kept in the hospital for four weeks or longer if necessary. We also keep all patients receiving anticoagulants in the hospital for the duration of such therapy. We have

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found that the desired degree of rest is often more readily and more uniformly enforced in the hospital: on one occasion one of us was unable to see a patient with an acute infarction when a visit was made to his home at an unexpected time because he was out for a ride!

Our patients with acute coronary occlusion are kept at bed rest from three to six weeks depending upon the severity of the case. The presence of the factors enumerated by Russek[1] and others which cause the patient to be classified as a bad risk will generally keep him in bed longer. On the other hand, the good risk patient is often allowed to use a bedside commode for bowel movements provided he is assisted, and he remains in bed a shorter length of time. During the first two weeks after onset we are more conservative in regard to rest even when dealing with the good risk patient; this period is regarded as a crucial one in the course of this disease. We agree with White[2] that undue activity increases the incidence of ventricular rupture during the first two weeks, and while a certain number of patients will expire in this period regardless of the treatment employed, it is better for them to die in bed than on the floor.

Since Levine's[3] advocacy of the "chair treatment" for myocardial infarction, there has been considerable discussion concerning this type of rest. We feel that the argument of bed rest versus chair rest is more apparent than real: there is little difference between our patient with the head of his bed elevated and the foot lowered and the patient sitting in a chair. We do not favor the chair rest because of the increased demands upon hospital personnel that lifting the patient in and out of bed entails; also, if a patient thinks he is well enough to sit in a chair, he may tend to think he is well enough to walk about or to do other things that he should not be doing. It should be noted that in most instances hospital bed rest is far from the "absolute bed rest" that is commonly ordered: most patients will move about in bed considerably; in fact, if they do not do so of their own accord, they should be encouraged to at least exercise their arms and legs to some extent. This of course does not apply to patients in shock or to those with extreme chest pain. In regard to the latter, we doubt that others would get these patients up in a chair, either.

It has been claimed that extended bed rest is harmful because it favors the development of thromboembolic phenomena. Our experience lends no support to this thesis; rather, it tends to disprove it. In our series[4] of 386 cases of acute myocardial infarction treated with relatively strict bed rest, and *without anticoagulants*, thromboembolic phenomena occurred in eight (2 per cent). Thrombophlebitis and phlebothrombosis have been extremely rare in our acute coronary patients, whether they received anticoagulants or not.

Diet has a bearing upon the ratio of cardiac rest to cardiac work, and this aspect of diet seems appropriate for inclusion in this discussion, even though the broader subject of diet in coronary disease is beyond the scope of this paper. It is well known that during the digestive process the supply of blood to the organs of digestion is increased to a considerable ex-

tent, hence, it is logical to restrict the diet both as to quantity and quality. The diet should be of the low calorie, low residue variety and a liquid diet may be advisable if the patient is critically ill. One objective should be to avoid straining at stool, since the exertion required by the latter may lead to serious consequences. Since patients at rest seem to have an inordinate amount of difficulty with gaseous distention of the gastrointestinal tract which in turn interferes with rest, foods which are prone to generate gas should be avoided. During the convalescent stage when the patient is semi-ambulant a light diet is preferred, and it is considered advisable for the patient to rest for at least a half hour after each meal in order to avoid the extra demands upon the heart resulting from digestion and exercise simultaneously.

Narcotics and sedatives may be necessary to secure adequate rest in an individual with pain, dyspnea, or extreme apprehension, but we feel that they are often prescribed far too freely; they are even prescribed routinely by some physicians. While we believe that rest is necessary, we see no reason to give narcotics to the patient who has become relatively asymptomatic merely to depress his activity to a rigor mortis level. In fact, as we have already inferred, such a procedure is probably harmful as it could lead to a higher incidence of thromboembolism. We have found the so-called tranquilizers to be of some value in helping the patient secure proper rest, but here again a word of caution is necessary: when prescribed they should be given under close supervision, particularly during the initiation of therapy when the patient's reaction to them is unknown. Some of the tranquilizers may have rather marked hypotensive effects in certain patients; we have observed two patients with acute infarcts who suffered a sudden drop in blood pressure and went into refractory shock subsequent to the initial dose of the drug.

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THE ELECTROCARDIOGRAM OF THE MONTH

The authors would be pleased to receive comment and controversy from readers in relation to explanations offered.

This electrocardiogram was obtained from a 58 year old white woman three days following an attack of severe pain in the chest. The pain did not radiate to the arms or any other characteristic area. There was no fever, no leucocytosis, and no increase in the sedimentation rate. She is not hypertensive and she does not have diabetes. The pain did not recur so that there was no opportunity to study an electrocardiogram made during pain at this time. Employing a polychannel apparatus electrocardiograms were recorded before and during carotid sinus stimulation. This was repeated with a second set of precordial leads made one interspace higher on the chest.

Interpretation

The original record *A* is not dissimilar to many normal electrocardiograms, even though T3 is higher than T1 in the presence of slight left axis deviation. If aVL had been recorded it would have shown an inverted T wave, but this finding means no more than the fact that TIII is greater than TI and is also encountered in many normal electrocardiograms. When we increased cycle length by carotid sinus stimulation the T wave in lead I became inverted while in leads V4 and V6 it became diminished in height and notched. When precordial leads were repeated at a higher level carotid sinus stimulation resulted in a definite inversion of a previously low T wave in V4 (itself a suspicious finding).

The record shows the value of studying the T waves of the electrocardiogram at different cycle lengths and how this can be accomplished by carotid sinus stimulation. In normal hearts a similar change in cycle length usually causes no change in the T waves or a slight *increase* in their size. Such a change as is recorded here is certainly more diagnostic of ischemia than is the record *A* alone. At the same time it should be observed that a slight lowering of the T wave in the left precordial leads when it occurs in older persons with carotid sinus slowing may not be of clinical significance. One must also warn against mistaking changes due to change in the respiratory phase for changes due to cycle length change. Many persons are apt to take a deep breath when the carotid artery is compressed.

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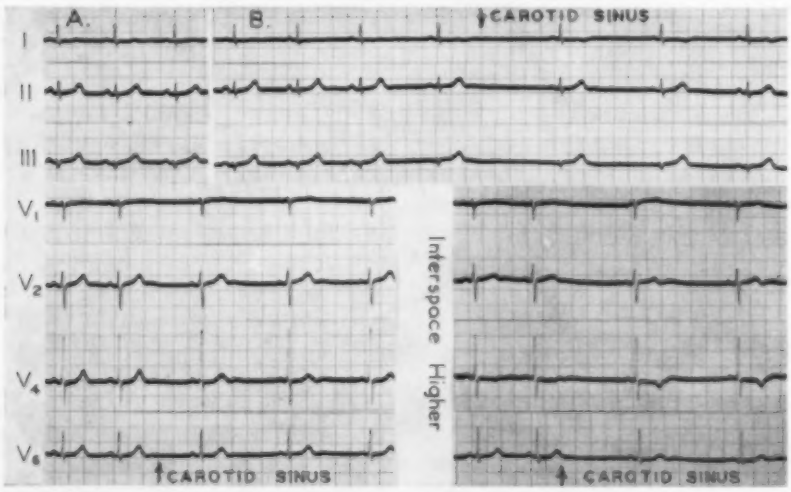

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Case Report Section

Xanthogranuloma as a Coin Lesion of the Lung*

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Isolated pulmonary xanthomatous nodules which present as coin lesions are uncommon. The gross resemblance of the lesion to a neoplasm and the peculiar microscopic characteristics, especially as seen in frozen sections, may lead to diagnostic errors. The following two cases are similar to those classified as xanthomas and reported by Scott, Morrow, and Payne[1] in 1948 and by Ford, Thompson, and Blades[2] in 1950. The lesion appears to be identical with the xanthogranulomas in the retroperitoneal region as described by Oberling[3] in 1935.

Case 1: (11087) A 10-year-old white boy was admitted to the National Jewish Hospital at Denver because an asymptomatic round mass was found in the upper lobe of the right lung by x-ray film six months before (Fig. 1). He was treated with streptomycin and para-aminosalicylic acid on the assumption that it was a solid tuberculous focus. Physical examination was negative. The x-ray picture remained unchanged, and the tuberculin, histoplasmin, and coccidioidin skin tests were negative. Laboratory procedures were negative; blood lipid studies were not done. At thoracotomy, a discrete nodule was shelled from the upper lobe of the right lung. As frozen sections showed a highly cellular lesion, this lobe was then resected. Recovery was uneventful.

The specimen consisted of a soft resilient pale yellow unencapsulated nodule which measured 2.5 x 3 cm. The right upper lobe appeared to be normal except for a cavity in the apical segment from which the lesion had been enucleated. Microscopically, the mass consisted of sheets of spindle-shaped and oval cells in fascicular arrangement with small blood vessels interspersed (Figs. 2 and 3). The nuclei were relatively large and vesicular with one or two nucleoli. Some nuclei were hyperchromatic. The cytoplasm was pale with faint minute vacuoles. Some syncytial-like groups of larger cells were scattered throughout, but typical reticulated xanthoma cells and giant cells were not observed. Occasional eosinophils and lymphocytes were present. Scharlach R. fat stain unexpectedly revealed large amounts of lipoid within the great majority of both the spindle and oval cells. Reticulum fibers outlined the many small blood vessels, and, in some fields, coarse parallel fibers were present among the cells containing lipid. The elastic fiber Van Gieson stain failed to reveal mature collagen or elastic tissue. The Weil and Bodian stains showed no nerve fibers. The margin of the lesion in the separately resected right upper lobe consisted of a fairly discrete zone of granulation tissue with many foam cells, neutrophils, plasma cells, nodules of lymphocytes, and relatively little collagen. The mucosa of an apical segmental bronchial branch was involved in the reaction.

Case 2: (89366) A 17-year-old white boy entered Colorado General Hospital for resection of a round lesion in the right lower lung field just above the diaphragm, which was found in a routine radiograph. Physical examination and routine laboratory studies revealed no abnormality. Blood lipid levels were not obtained. At thoracotomy, a sharply circumscribed spherical nodule, unrelated to bronchi, was shelled from the lower lobe of the right lung. His postoperative course was uneventful.

The specimen consisted of a gray-yellow, homogeneous, soft, slightly bosselated spherical nodule measuring 1.8 cm. in diameter. Microscopically, it was composed of compact fasciculated spindle-shaped or oval cells with finely vacuolated cytoplasm. The nuclei were plump, pale or darker, with fine evenly distributed chromatin. Lymphocytes, plasma cells, and larger histiocytes were scattered throughout. Typical

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large xanthoma cells were numerous in several fields (Fig. 4). The reticulum stain outlined many small blood vessels throughout the lesion, but fibers between cells were rare. Mature collagen was present only in occasional patchy peripheral foci.

Discussion

These discrete soft pale yellow nodules were composed predominantly of spindle-shaped cells which resembled fibroblasts. For this reason the diagnosis of a fibroblastic tumor was suggested. However, stains for connective tissue revealed only rare foci of collagen. One of the lesions contained intercellular reticulum; reticulum fibers were generally confined to walls of the many small blood vessels. It is of interest that a significant component of collagen was absent in the lesion of a previously reported case.[2] The abundance of lipoid material was recognized only with the use of the stain for fat. The phagocytic character of the cells might have been suspected from the fine foamy cytoplasmic vacuolation of most of the cells. Typical xanthoma cells were present in a few fields in Case 2; giant cells were absent. Leukocytes were present in varying numbers. The pulmonary framework was destroyed; the mucosa of a bronchial branch was partly replaced with granulation tissue.

We have classified these lesions as xanthogranulomas because they appeared to represent a genuine granulomatous reactive process, basically identical with that described by Oberling[3] in three retroperitoneal lesions. The relationship of the pulmonary form of the disease with the retroperitoneal lesions was pointed out by Stout[4] who studied material from Case 1. Stout[5] noted the occurrence of xanthogranulomas in the mediasti-

FIGURE 1 (Case 1): X-ray taken six months prior to admission.

num and mesentery as well as in the lung and retroperitoneal region. Although the term xanthogranuloma does not emphasize the pseudoneoplastic quality of the process, we prefer it to others which have been used. The term xanthoma indicates a uniform proliferation of characteristic foam cells. Fibroxanthoma or xanthofibroma seem to be less appropriate terms as they imply a neoplastic origin, and collagen fibers also are sparse in the nodules.

Oberling stated that xanthogranulomas are frankly inflammatory, consisting of more or less extensive infiltrations of macrophages, lymphocytes

FIGURE 2

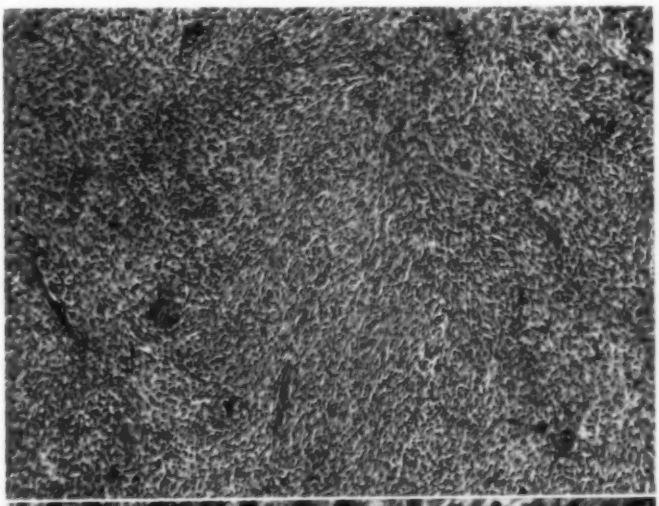

FIGURE 3

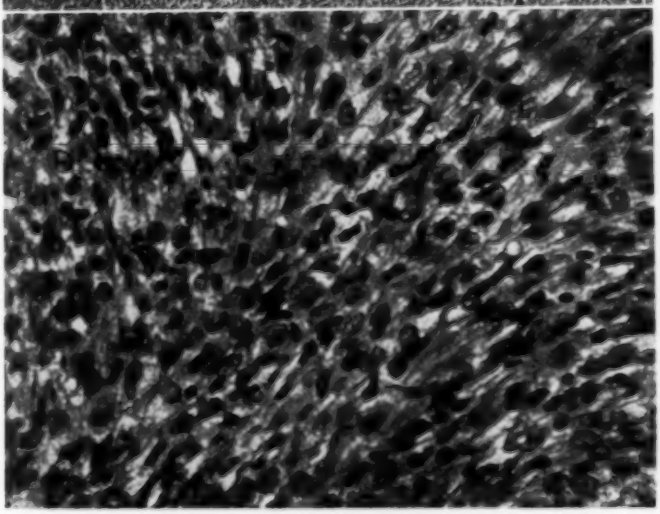

Figure 2 (Case 1): Bundles of spindle-shaped cells. H. & E. ×100.—*Figure 3* (Case 1): The foamy character of the cytoplasm of the elongated cells is shown. H. & E. ×400.

and plasma cells, areas of sclerosis, and invariably foam cells containing neutral fat and cholesterol. One of his three cases exhibited a pseudosarcomatous pattern. He related the disease to that of Hand-Schuller-Christian and noted that such isolated granulomas had been described in bones, lymph nodes, the stomach, and elsewhere. He considered them to be distinctly different from the xanthomas of skin, tendon sheath, and joints which were associated with jaundice, diabetes, or generalized disturbances of fat metabolism. They were not simply a reaction to lipid such as occurs in Niemann-Pick's disease. They also differed from the xanthomatous transformation of nerve sheath tumors. Oberling further believed that local irritative inflammation and derangement of cholesterol metabolism were both significant factors in pathogenesis. In his cases as in ours no clue to a specific infective agent was noted.

More recently, Umiker and Iverson[6] added three intrapulmonary postinflammatory "tumors" to the literature and included those of Scott et al,[1] Ford et al,[2] Csermely's[7] case of xanthofibroma, and Childress and Adie's[8] plasma cell tumor in a review of the problem. They considered that all of these lesions were inflammatory on the basis of microscopic appearance or history. If one cell predominated, they simulated xanthoma, fibroxanthoma, neurofibroma, vascular tumor, or plasma cell tumor. These nodules were similar to three nonxanthomatous lesions of the pleura described by Brown and Johnson.[9] We believe that the lesions we have called xanthogranulomas are the same as several of the postinflammatory "tumors". Nevertheless, as the xanthomatous feature was dominant, the

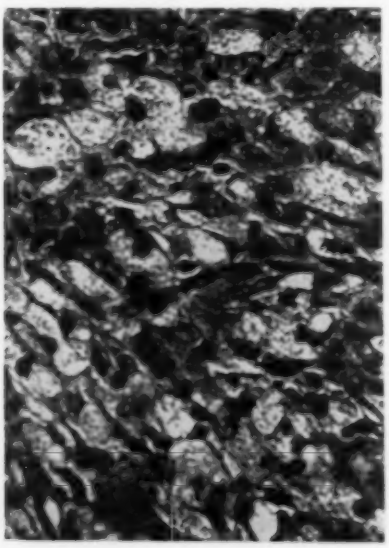

FIGURE 4 (Case 2): Field of typical xanthoma cells. H. & E. × 400.

more specific descriptive diagnosis of xanthogranuloma appears to have merit, at least in certain cases.

The sclerosing hemangiomas of the lung reported by Liebow and Hubbell [10] also showed xanthomatous elements. These vascular lesions, regarded as analogous to those of the skin, exhibited hemorrhages, papillary infoldings, and obliteration of air spaces with atypical proliferation of lining cells. The authors concluded that the relationship to the so-called xanthomas or postinflammatory "tumors" must be considered tentative.

Two cases of a peculiar xanthomatous nodule of the lung have been reported because their superficial resemblance to a neoplasm offers a diagnostic problem and because they probably will be observed more frequently with the increasing tendency to extirpate coin lesions. They are termed xanthogranulomas because of the basic granulomatous nature of the cellular proliferation, the heavy lipoid content of the constituent cells, and the similarity to the lesion as seen in other locations. These two cases appear to be either variants or identical with the other seven cases in the literature which have been called postinflammatory "tumors" by Umiker and Iverson. The inflammatory origin seems to be common to all. Oberling believed local inflammation and a derangement of cholesterol metabolism were important. Association with a general disturbance of lipoid metabolism has not been noted in any of the cases, although sufficient laboratory investigations have not been made to exclude this possibility. As yet there is no certainty that the lesions are related to Hand-Schuller-Christian disease as considered by Oberling or to eosinophilic granuloma of the lung. The prognosis appears to be good, and symptoms are either absent or mild.

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Spontaneous Mediastinal Emphysema with Bilateral Pneumothorax as a Complication of Bronchopneumonia*

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Spontaneous mediastinal emphysema with bilateral pneumothorax as a complication of bronchopneumonia has not, to our knowledge, so far been reported in the literature.

Gray[4] in 1919 presented a case of bilateral spontaneous pneumothorax occurring in the course of advanced bilateral tuberculosis after which the patient soon died. In a second case of spontaneous mediastinal emphysema with bilateral pneumothorax,[6] no clinical or radiological findings which could explain the etiology were discovered.

This 17 year old boy was born in Israel. Family and past history were irrevelant. He fell ill a week before admission to the Haifa Rambam Hospital, complaining of pyrexia, headache and chest pains which increased on deep inspiration. His general condition was fair until 24 hours prior to admission when he suddenly felt worse.

On the day prior to admission there had been a sudden attack of severe cough, followed by intense pain in the centre of the chest, accompanied by marked dyspnoea.

On examination he appeared acutely ill, and had severe dyspnoea, orthopnoea and considerable cyanosis of lips, ears and fingertips. Pronounced râles during respiration were heard from a distance and scummy spittle was dripping from his mouth. The clinical picture resembled that seen in pulmonary edema. He was restless and mumbling unintelligibly.

His blood pressure, when first examined, was 150/0, pulse-rate 130 and temperature 38° C. Moist râles were heard in both lungs which made it difficult to hear the heart-sounds or to define their nature. The breath-sounds over both upper lung fields were diminished and on percussion cardiac dullness could not be determined.

The abdomen and extremities were negative.

ECG findings on admission: sinus tachycardia 148'. High P in the leads L II, L III and AVF and negative in AVL. (An ECG four days later showed normal findings.)

He was immediately given 0.5 mg. strophantin and 0.01 morphine intravenously and was placed in an oxygen tent, but almost no change in his condition was observed.

During the night a venopuncture of 500 cc. was performed and his condition improved slightly. The next day the respiratory distress was still present and there was a tachycardia of 130 per minute. The temperature remained unchanged and the blood pressure was then found to be 140/80.

Subcutaneous emphysema was found in the region of the neck and above the clavicles on both sides. Cyanosis persisted and the respiratory sounds remained weak in the apical regions. There was hyperresonance to percussion over both lungs.

In the region of the midchest, strange, crunching breath-sounds were heard, as well as noises resembling the bursting of toy balloons. These unusual sounds were best heard above the precordial area. He complained of oppression of the chest and difficulty in breathing, which was aggravated by every movement.

The x-ray film examination of the chest showed pneumothorax on the right side with compression of the entire lung by a mantle of air, about 2 cm. in width. On the left there was pneumothorax in the apical region. Mediastinal emphysema and subcutaneous emphysema of the neck and the supraclavicular areas were seen.

The lung fields showed a veiling, composed of soft, ill-defined patches with a dense and almost homogeneous clouding at the base of the right lung and in the left upper lung field.

These findings suggested bilateral bronchopneumonia, mediastinal emphysema, bilateral pneumothorax and subcutaneous emphysema.

Throughout the day his condition remained poor. He was cyanotic and considerably dyspnoeic and as there seemed to be no tendency to improve, pleural puncture was performed in the evening. The needle was introduced first on the right side and the

*"Rambam" Government Hospital.

intrapleural pressure was found to be 140 mm. Hg. Approximately 1,000 cc. of air was withdrawn and the pressure came down to —0. The same procedure was carried out on the left, the pressure was 10 mm. Hg., and after withdrawal of 400 cc. of air it decreased to —0. His condition improved immediately.

An x-ray film at that stage showed no pneumothorax on the right side, but there still was air over the left apex. The mediastinal and subcutaneous emphysema remained unchanged and the lungs still showed the bronchopneumonic infiltrations.

His general condition continued to improve, but the temperature remained elevated in spite of continuous treatment with penicillin and streptomycin. The temperature subsided only after chloromycetin treatment was begun. Repeated throat and sputum smears revealed pure cultures of staphylococcus aureus sensitive only to chloromycetin.

X-ray films on the third day of hospitalization showed many ill-defined and confluent, soft infiltrations on both sides. There were still remnants of the pneumothorax at the left apex, pneumo-mediastinum and subcutaneous emphysema in the cervical region. There was no further important roentgenological change on the fourth day. On the seventh day the x-ray film still showed evidence of bronchopneumonic infiltrations, but no more signs of the pneumothorax or the mediastinal and subcutaneous emphysema. On the 16th day of hospitalization no evidence of chest disease was found.

The clinical entity of spontaneous mediastinal emphysema has been known for many years.[1] Apart from those cases, in which mediastinal emphysema appears following trauma or operation, and which should not in a strict sense be described as "spontaneous," there are many other possibilities as to its etiology: Its occurrence as a complication of infections (tuberculosis, pneumonia, diphtheria, influenza, measles, pertussis, asthma, during labour[3, 4, 10] and in obstructive emphysema) has been described, but there remain not infrequent cases in which the cause is unknown and which are designated as "idiopathic."

The most striking clinical finding is known as "Hamman's syndrome" or "sign," which is described as a loud, crunching, crackling, snapping, crepitant sound, synchronous with the heart beat.[5] Cardiac dullness is partly or completely obliterated. Mediastinal emphysema is often accompanied by pneumothorax, most commonly found in the left upper region. The latter is described in nearly all cases as being so limited as to be detected only on x-ray film.

Various clinical symptoms, often contradictory, are described by different authors, possibly on account of the respective varying etiology. On the other hand, the clinical manifestations are largely due to the measure of the physical changes, i.e., the amount of air in the mediastinum or the size of the pneumothorax. Since the number of cases seen by individual authors is generally small, generalizations in their description were sometimes used, which were perhaps not quite justified by these sporadic observations.

One of the main and most common symptoms is a sudden severe pain in the chest, which may disappear within hours, but might continue for days, and which, depending on its immediate cause, i.e., the amount and localization of mediastinal air, may even simulate an attack of angina pectoris. The pain, in the opinion of some authors,[2, 7, 10] et al is caused chiefly by the pressure of air which intruded suddenly between the heart and the anterior chest wall. Its presence in large amounts, according to them, is liable to cause compression of the heart and large vessels. These authors explain that encroachment upon the space occupied by the pulmonary vessels interferes with the circulation through the lungs and may result in embarrassment to the right heart. In this case, Klein[7] reports

that characteristic ECG findings of acute right ventricular strain are demonstrated, whereas Stein[10] found that there are no typical electrocardiographic changes in this condition.

Again, while Klein[7] describes the above mentioned right heart strain and others confirm the occurrence of cyanosis as a rather frequent symptom. Schendstock[9] reports that "shock and cyanosis do not occur" and Miller[8] came to the conclusion that "dyspnoea, cyanosis and orthopnea may occur, but are not characteristic."

CONCLUSIONS

The presentation and discussion of this case appears justified for the following reasons:

a) The rare occurrence of the syndrome;
b) The typical clinical findings which could lead to its correct diagnosis;
c) The possibility of a specific treatment consisting of the withdrawal of air from the pleural cavity in order to decrease the extent of the pneumothorax.

The marked release from discomfort, which the patient experienced following this intervention is astonishing, if compared to the comparative ease with which therapeutic pneumothorax is tolerated, even though the amount of air which is normally introduced is generally far greater than was found in this case. The explanation for this discrepancy is believed by us to be the simultaneous mediastinal emphysema, which causes compression of the heart and thereby diminished cardiac output with resulting circulatory failure, together with the pressure exercised by the pneumothorax upon the distended mediastinum. We have no explanation for the blood pressure abnormality, which on repeated examinations at the time of admission was found to be similar to that seen usually in aortic insufficiency, arterio-venous fistula, etc., and which returned to normal later on.

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Chemotherapy of Specific Infectious Diseases of the Lower Respiratory Tract

Report of Committee on Chemotherapy and Antibiotics
American College of Chest Physicians

The majority of pulmonary infections can be successfully treated by the judicious use of antibiotics and other chemotherapeutic agents. It is important to establish a diagnosis of the type of infection in all infectious diseases of the respiratory tract. Cultures should be made prior to therapy whenever feasible. Sensitivity tests of the organisms found in all prolonged infections are essential guides in the care of the patient. It is sometimes difficult to make an exact bacteriological diagnosis at the onset of a pulmonary infection, and treatment may have to be started at once. A simple Gram's stain of a fresh sputum specimen is important in determining the type of therapy while awaiting the cultures. If the diagnosis is still obscure and the patient has a severe infection, therapy designed against both gram-positive and gram-negative organisms should be instituted. Obviously all other clinical guides will be useful, such as the manner of onset of the disease, the characteristics of the sputum, the white count, the cold agglutinins, etc. Treatment should be vigorous and should be continued until all signs of infection have cleared. This is important to prevent development of chronic disease of the lungs and bronchi.

Classification of Pneumonias

I. *Bacterial*
- a. Pneumococci
- b. Streptococci
- c. Staphylococci
- d. Klebsiella Pneumoniae
- e. Hemophilus Infections
  1. Pertussis
  2. H. Influenzae
- f. Pasteurella Infections
  1. Pasteurella Pestis
  2. Pasteurella Tularensis
- g. Coliform, Proteus and Pseudomonas (gram-negative bacilli present in the intestinal tract)
- h. Salmonella Group
  1. Typhoid
  2. Paratyphoid A.B.C.
- i. Brucella
- j. Anthrax
- k. Glanders

II. *Viral* (Known and Probable)
- a. Psittacosis
- b. Influenza A & B
- c. Variola
- d. Varicella
- e. Rubella
- f. Lymphocytic Choriomeningitis
- g. Primary pneumonitis of infants
- h. Infectious mononucleosis
- i. Erythema Exudativum Multiforme
- j. Primary atypical pneumonia

III. *Rickettsial*
- a. Typhus
- b. Rocky Mountain Spotted Fever
- c. Q Fever

IV. *Mycoses* (Producing a pneumonia-like picture)
- a. Actinomycosis
- b. Nocardiosis
- c. Blastomycosis
- d. Coccidiodomycosis
- e. Histoplasmosis
- f. Moniliasis
- g. Cryptococcosis
- h. Aspergillosis
- i. Geotrichosis
- j. Penicilliosis
- k. Sporotrichosis

Treatment of Pneumonias

I. Bacterial Pneumonias

Pneumococcal Pneumonia. Penicillin is the drug of choice in the treatment of pneumococcal pneumonia. It is best given by the intramuscular route, using 300,000 units of aqueous penicillin every three to four hours, or 600,000 units of procaine twice daily. Oral penicillin is not advised except in mild cases. Therapy is continued until the temperature has been normal for three days. Larger or smaller doses may be used depending on the severity of the disease. The sulfonamides are highly effective in the treatment of pneumococcal pneumonia. The dosage is 6 to 8 gms. daily. The broad-spectrum antibiotics, including tetracycline, chloramphenical and erythromycin are all effective, but should still be considered second to penicillin.

Streptococcal Pneumonia. Treatment of streptococcal pneumonia is the same as that of pneumococcal pneumonia.

Staphylococcal Pneumonia. Treatment of staphylococcal pneumonia requires considerable care in view of increasing development of staphylococcal resistance to most antibiotics. Sensitivity tests should be made early. If the organism is penicillin sensitive, large doses of penicillin, two to

four million units daily should be given and no other antibiotic need be given with it except perhaps streptomycin. If the organism is penicillin resistant and susceptible to erythromycin or novobiocin then one or the other of these drugs should be used. Vancomycin, which is not yet on the market, is an excellent bactericidal agent for staphylococci and should be used if the organism is resistant to other more readily available drugs. In the seriously ill patient who is not responding to the prescribed therapy, bacitracin in doses of 25,000 units every six hours should be added. The nephrotoxic potentialities of bacitracin must be watched. Treatment of staphylococcal infections should be prolonged for three or four weeks.

Klebsiella Pneumonia. Test of susceptibility should be performed but usually this type of pneumonia is best treated by streptomycin 2 to 4 gms. daily plus one of the tetracyclines in 4 gm. dosage initially. After response to therapy the dosage may be lowered. Sulfadiazine has also been quite effective in conjunction with streptomycin. Treatment must be continued for several weeks because of the severity and chronicity of the disease. The potential toxicity of streptomycin when used too long must be kept in mind.

Hemophilus Infections. Chloramphenicol or tetracycline in doses of 2 to 4 gms. daily are effective in both pertussis and H. influenzae infections. Sulfadiazine or streptomycin should be used in combination in the serious case.

Pasteurella Infections. Sulfadiazine, streptomycin, chloramphenicol and tetracycline have all proved effective in the treatment of plague pneumonia. Streptomycin is the drug of choice. Streptomycin is the ideal agent in the treatment of tularemic pneumonia in dosage of 2 to 4 gms. daily. The broad spectrum antibiotics are also effective.

Coliform, Proteus and Pseudomonas Group. This group is becoming increasingly important as a result of antibiotic therapy. Sensitivity tests must be done to find the most effective drugs. The organisms may be sensitive to the broad-spectrum antibiotics, sulfadiazine and streptomycin. A tetracycline may be sufficient for the coliform and proteus types of pneumonia if the organism shows susceptibility to these agents but combinations of antibiotics are usually necesssary. If these organisms are resistant combination of tetracycline and streptomycin in full dosage should be tried. If response does not occur penicillin, in large doses, in combination with chloramphenicol should be tried. In resistant infections polymyxin may be used with a tetracycline. Polymyxin is the drug of choice for pseudomonas pneumonia. The drug is both nephrotoxic and neurotoxic. It should be used with caution. In general, infections by this group respond poorly to all antibiotics.

Salmonella Group. The typhoid bacillus is a rare cause of pneumonia. Chloramphenicol 2 to 4 gms. daily followed in a few days by 1 gm. dose is specific. In the other Salmonella infections, chloramphenicol or one of the tetracyclines may be used.

Brucella Infections. Brucella infections are best treated by a combination of tetracycline, ¾ gm. every six hours in combination with streptomycin 1 gm. daily for a month.

Anthrax. Pulmonary anthrax is a rare complication of anthrax but when present is a very serious and fulminating disease. The tetracyclines are the drugs of choice, though penicillin and the sulfadiazines have also been used successfully.

Glanders. Lung lesions occur in about one-quarter of the glanders cases. Sulfadiazine and streptomycin are effective in the treatment of glanders. The broad-spectrum antibiotics have also been used successfully.

II. Viral Pneumonias

Psittacosis. The tetracyclines are the drugs of choice using 4 gms. daily for the first two days, followed by a 2 gm. daily dosage. Penicillin has been used successfully.

Virus Influenzal Pneumonia. There is no known specific for influenzal pneumonia.

Variola. Pulmonary lesions often occur in smallpox. There is no specific for the primary disease but because of secondary infections by bacteria appropriate chemotherapy for these infections should be used.

Varicella. Pneumonia occurs rarely. Treatment should be directed to secondary bacterial infections.

Rubella. Bronchopneumonia is a common complication of measles. While there is no specific for the measles virus, superimposed bacterial infections are frequent and can be successfully treated by penicillin or the tetracyclines.

Lymphocytic Choriomeningitis. Pneumonia occurs in lymphocytic choriomeningitis. Treatment is symptomatic.

Primary Pneumonitis of Infants. There is a serious disease in the newborn and premature infants probably due to a virus. There is no known specific therapy.

Infectious Mononucleosis. Bronchopneumonia is a rare complication of infectious mononucleosis. There is no known specific for this disease.

Erythema Exudativum Multiforme (Stevens-Johnson Syndrome). Pneumonia is a common accompaniment of this disease. It appears to be due to a virus which is not affected by any known antibiotic. Steroid therapy has often proven to be helpful.

Primary Atypical Pneumonia. The status of drug therapy of Primary Atypical Pneumonia is still under question. Some observers feel that a tetracycline 0.5 gm. every six hours should be given until temperature has been normal for at least three days, principally to guard against secondary bacterial invaders. Some observers prefer to use no antibiotic therapy in the average case unless there is indication of a secondary infection.

III. Rickettsial Pneumonias

Treatment of all of the rickettsial pneumonias may be combined together. Chloramphenicol or a tetracycline appears to be equally effective. The dosage in severe cases is 1 gm. every six hours for three doses, then 0.5 gm. every six hours until the temperature is normal.

IV. Mycotic Infections

Actinomycosis. Penicillin is the drug of choice, one or two or more million units a day usually along with surgical drainage if necessary. One of tetracyclines may be just as effective. Treatment is continued for at least six weeks and should be kept up long after the lesions have disappeared to prevent a recurrence.

Nocardiasis. Sulfadiazine is the drug of choice for nocardia infections. The broad-spectrum antibiotics may be helpful. The treatment must be prolonged.

Histoplasmosis. At present there is no proven therapeutic agent for this disease, but very suggestive results are being obtained with a new antibiotic, amphotericin B. The drug has been employed in a number of cases and the incidence of serious toxic manifestations has been relatively low. It has also demonstrated definite therapeutic effect. The drug is very difficult to administer and must be given intravenously in a slow drip over a period of six hours. Approximately 1 mgm. per kilo per day is the usual daily dose and treatment is continued from 30 to 60 days. Under special circumstances the daily dose may be increased to as much as 100 mgm. per day. An oral form of the drug is available, but has not proved to be effective. Immediate febrile complications during therapy are not unusual especially if the drug is given too fast. These effects may be ameliorated by aspirin. These reactions have not interfered with the continued use of the drug.

Blastomycosis. 2-hydroxystilbamidine is the most effective agent in the treatment of blastomycosis. Standard daily dose is approximately 250 mgm. dissolved in 250 to 500 cc. of 5 per cent dextrose, and given intravenously. This is given rather slowly over a period of several hours at least. The drug should be used immediately after preparation and the solution should be protected from sunlight. Thirty to sixty days of daily dosage of 250 mgs. is recommended. The drug may be repeated in case of a relapse. Facial neuropathy may occur but is much less frequent than with stilbamidine. Recently amphotericin B has appeared quite effective in treatment of Blastomycosis.

Coccidioidomycosis. Amphotericin B may be used for treatment of coccidioidal disease.

Moniliasis. Mycostatin is an effective antifungal drug for intestinal moniliasis, or it can be used locally. It has no effect on the systemic disease as it is not absorbed from the intestinal tract. In systemic moniliasis it is suggested that one of the newer antibiotics be employed, such as amphotericin B.

Cryptococcosis. Amphotericin B may be used. Its effectiveness is still under investigation.

Aspergillosis, Geotrichosis and Penicilliosis. These diseases are refractory to all known antibiotics. Amphotericin B should be tried.

Sporotrichosis. This usually responds satisfactorily to potassium iodide. 2-hydroxystilbamidine should be tried in the refractory case.

Steroid Therapy

The role of steroids in the therapy of infectious disease is a subject of tremendous controversy. When overwhelming infections cause adrenal insufficiency steroid therapy is indicated. The beneficial anti-inflammatory and "antitoxic" effect of the steroids is opposed by the adverse influence of the steroids on tissue localization of infection. However it is likely that one may accomplish the desirable and prevent the potential harmful effects of steroids by the simultaneous use of anti microbial agents to which the infective agent is susceptible. On theoretical grounds at least it would be undesirable to use steroid therapy in infections caused by organisms resistant to anti-microbial agents. There appears to be a place for the use of steroids in overwhelming infections not responding to conventional therapy.

Committee on Chemotherapy and Antibiotics
American College of Chest Physicians

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Editorial

"And he said unto him, if they hear not Moses and the prophets, neither will they be persuaded, though one rose from the dead." St. Luke, 16:31

The exemplary effort of the American College of Chest Physicians in sponsoring international congresses on diseases of the chest throughout the world has contributed to a most successful scientific interchange and has linked physicians around the globe in a spirit of understanding in non-medical fields. These ties have brought home to us that we are part of a corps of a million and a half men and women motivated by the ideal of conserving life. Even more closely must the ideal of conserving happiness unite us, for we cannot conceive of health without the happiness that springs from mental health. The physician is a champion of the struggle against disease, death and unhappiness.

In constant collision with the persistent, heroic and tireless labor of the physicians of the world is the menace of disease, death and unhappiness represented by war. War is an everyday theme; every day the newspapers speak of war; every day the motion pictures throw it on their screens; every day we listen to the radio, fearful lest some cultural program be interrupted by an announcement that the baleful tempest has been unleashed.

From all parts of the world, editorials in this journal — A. Omodei Zorini's from Italy, Jose Baldo's from Venezuela, Jay Arthur Myers' Arnold S. Anderson's and Andrew L. Banyai's from the United States, Richard R. Trail's from England, and Mohammed Ibrahim's from Pakistan — tell us eloquently how united are the aspirations and acts of physicians in furthering human understanding. No peaceful task is more rewarding than the discovery by combined effort of new arms against disease; no collaboration is greater than that which united Noguchi, Metchnikoff, Calmette, Fleming, Waksman, Finlay and many others.

Physicians, however, need no persuasion to appreciate the benefits of mutual interchange or the nobility of a united medicine. It is the masses and their leaders who need be persuaded of the truth in the ideals that we proclaim. Man must not go on working his own destruction, for armament in its present perfection can only lead to annihilation of the human race and an infinite retrogression of civilization.

When we are told that interplanetary space will soon be conquered and that the day is not distant when man will tread the moon, we turn disconsolate eyes to earthly conquests that concern us more closely; conquests of cancer, tuberculosis and the ever-increasing psychoses that fill half the hospital beds of the civilized world.

Profoundly disturbed, we see that the lunacies of civilization drive man to fratricidal combat, and that not even exposition of his motives offer

a remedy for avoiding war. Man has begun to fear freedom. He escapes from liberty, as Fromm says, because he has created for himself a state of mind in which warlike tendencies enslave him.

This is the world's sickness. We physicians are accustomed to struggle with disease of individuals, but we have not yet confronted the problem of mass disease, the neurosis of agression that one can perceive in the mass subconsious mind. This is the problem that the medical profession finds before it. We must busy ourselves with its difficult solution, but how can we approach it with only our goodwill, our ethics and our unarmed, passive attitude? Precisely because we have these arms of kindness can we gradually modify the world, cause the masses to understand this evil and to face it.

Nothing is as good as going back and forth from one country to another, so that we may know and learn to love one another.

We are no prophets. Even Abraham recognized the futility of raising his voice to persuade people. We physicians must act by patiently spreading understanding among ourselves; we must foster international interchange and international aid in solving these problems. Wherever the physician can make his voice heard (and he has opportunities always and everywhere) his mission should be to promote mutual aid, of one country and one continent to another.

If strong and rich nations aid the dispossessed to rid themselves of the scourge of disease, their efforts will do more to promote peace than any other persuasive force.

We do not need more shipments of arms or money, but more help to conquer disease, ignorance and hunger in underprivileged countries! For it is desolating that while some may listen to the faint signals of an artificial satellite, others are awakened from their very sleep by cold and hunger.

*Donato G. Alarcon, M.D., F.C.C.P.**
Mexico D.F., Mexico

*Regent for Mexico

The President's Page

A glimpse into the following pages should suffice to whet the appetite of any College member who has not already formulated plans to attend the 24th annual meeting in San Francisco from June 18 through 22, 1958. The outstanding scientific program which follows is indeed a tribute to the labors of the Committee on Scientific Program and the able leadership of co-chairmen, Drs. Peter A. Theodos and Samuel Bellet. The diligence of effort and intensiveness of thought which have gone into the planning of this program are attested to by the high calibre of material and speakers throughout this program.

It has been most gratifying to observe the manner in which the scientific programs of the College meetings have grown and diversified through the years in adaptation to the growth and consequent diversification of membership interests. The constant demand to keep pace is being met with an eye already cast well into the future.

The new horizons which now beckon to all mankind as we plunge even deeper into the jet age offer a particular challenge to the physician specializing in diseases of the chest. Taking full cognizance of the aroused interest in this new field, our program committee has included a panel on "The Jet Age and Chest Medicine" in which the role of the chest specialist in this new era is expanded upon.

It is evident that no effort has been spared in securing authorities of international repute as speakers and panelists to present and discuss a variety of topics tailored to the specific interests of our members. No member who looks over the program on these pages can fail to find numerous topics which fall within his own particular field of interest whatever it may be.

The same high standards and diversity obtain in the fireside conferences and luncheon meetings which promise the top flight attractions those who regularly attend our meetings have come to expect. Many members in the past have been disappointed in being unable to secure luncheon tickets for the round table discussions. Keen interest in these luncheons has resulted in an overwhelming demand for the limited space available. Therefore to avoid this disappointing experience, I urgently recommend to all members that they send in their luncheon reservations as early as possible.

The Committee on Scientific Program and co-chairmen, Drs. Theodos and Bellet, are deserving of our sincere thanks for a splendid achievement in preparing such a standout program for the meeting this year.

Every doctor recognizes the fact that the role of a member of the medical profession in society extends far beyond the field of medicine. The doctor of today is a citizen of the world and his influence is felt around the globe. Through attendance at meetings, reading journals, and correspondence, he engages in a constant exchange of information and ideas which contribute in many ways to the shaping of tomorrow's world. No issue today takes precedence over that of world peace. Recognizing our role in this vital issue, *Diseases of the Chest* has embarked on a series of editorials on the topic of "The Doctor and World Peace" written each month by members of the College in different parts of the world.

The "World Peace" editorial appearing in this issue is by Dr. Donato G. Alarcon, Regent, Mexico City. This editorial was chosen for publication in the April issue as part of our salute to Pan-American Week, April 13-19. The College has a deep interest in Latin America since among our 6000 members there are 895 members representing every country in this area.

In line with the global interests of the College, I wish to remind you of the Fifth International Congress on Diseases of the Chest, September 7-11, 1958 in Tokyo, Japan. I cannot urge you strongly enough to attend this outstanding Congress which, in addition to offering a superb scientific program, promises to be a truly memorable experience for all.

Burgess L. Gordon

24th ANNUAL MEETING
AMERICAN COLLEGE OF CHEST PHYSICIANS
FAIRMONT HOTEL, SAN FRANCISCO

SEMINARS

Wednesday, June 18

Morning Sessions—9:00 a.m.

AM-1 PULMONARY DISEASE (MEDICAL)

Chairman:

James Kieran, Clinical Instructor in Medicine, Stanford University, School of Medicine, San Francisco, California

9:00 A.M.—The Principles of Pulmonary Physiology As They Apply to Clinical Medicine

Robert B. Stonehill, Major USAF (MC), Chief, Pulmonary Disease Service, and Pulmonary Physiology Laboratory, 3700th USAF Hospital, Lackland Air Force Base, Texas

9:35 A.M.—Sarcoidosis

Marvin S. Harris, Clinical Professor of Thoracic Diseases, College of Medical Evangelists, Los Angeles, California

10:10 A.M.—Mucoviscidosis

Paul E. Wilson, Assistant Clinical Professor of Pediatrics, Stanford University, School of Medicine, San Francisco, California

10:45 A.M.—Trends in Allergic Diseases of the Chest

Ralph Bookman, Instructor in Medicine, University of Southern California, School of Medicine, Los Angeles, California

11:20 A.M.—Current Concepts in Coccidioidomycosis

William Winn, Medical Director, Tulare-Kings County Sanitarium, Springville, California

A ten-minute question and answer period will follow each lecture

AM-2 CARDIOLOGY (SURGICAL)

Chairman:

Sanford Leeds, Assistant Clinical Professor of Surgery, University of California, School of Medicine; Associate Chief of Surgery In Charge of Cardiac Surgery, Mt. Zion Hospital, San Francisco, California

9:00 A.M.—Physiologic Evaluation of Patients for Cardio-Vascular Surgery

Elliott Rappaport, Assistant Clinical Professor of Medicine, University of California, School of Medicine; Director, Cardio-Pulmonary Laboratory, Mt. Zion Hospital, San Francisco, California

9:35 A.M.—Surgical Treatment of Congenital Heart Disease

Benson Roe, Assistant Clinical Professor of Surgery, University of California, School of Medicine, San Francisco, California

10:10 A.M.—Surgical Treatment of Acquired Heart Disease

Elmer C. Rigby, Chairman, Cardio-Thoracic Surgery Section, Queen of Angels Hospital, Los Angeles, California

10:45 A.M.—Surgical Approach to Coronary Artery Disease

Alfred Goldman, Attending Thoracic Surgeon, Cedars of Lebanon Hospital, Los Angeles; Director, Thoracic and Cardiac Hospital, City of Hope Medical Center, Duarte, California

11:20 A.M.—Surgery of Extra-Cardiac Vascular Anomalies

Paul C. Samson, Associate Consultant in Thoracic Surgery, University of California, School of Medicine, San Francisco, California

A ten-minute question and answer period will follow each lecture

Please complete reservation form on page 466

Seminars (continued)

Afternoon Sessions—2:00 p.m.

PM-1 PULMONARY DISEASE (SURGICAL)

Chairman:

Thomas B. Wiper, M.D., Thoracic Surgeon, San Francisco, California

2:00 *P.M.—Bronchopulmonary Segmental Anatomy*

Ian W. Monie, Associate Professor of Anatomy, University of California, School of Medicine, San Francisco, California

2:35 *P.M.—Surgical Treatment of Bronchogenic Carcinoma*

H. B. Stephens, Associate Clinical Professor of Surgery, University of California, School of Medicine, San Francisco, California

3:10 *P.M.—Surgical Approach to Treatment of Emphysema; Physiologic Aspects*

Roger H. L. Wilson, Assistant Clinical Professor of Medicine, University of California, School of Medicine, San Francisco, California

3:45 *P.M.—Surgical Aspects in the Treatment of Emphysema*

Orville Grimes, Assistant Professor of Surgery, University of California, School of Medicine, San Francisco, California

4:20 *P.M.—Changing Trends in Surgical Treatment of Tuberculosis*

David J. Dugan, Clinical Instructor in Surgery, Stanford University, School of Medicine; Consultant in Thoracic Surgery, Oakland Veterans Administration Hospital, San Francisco, California

A ten-minute question and answer period will follow each lecture

PM-2 CARDIOLOGY (MEDICAL)

Chairman:

Eliot Corday, Assistant Clinical Professor of Medicine, University of California at Los Angeles; Chief, Cardiac Clinic, Cedars of Lebanon Hospital, Los Angeles

2:00 *P.M.—Evaluation and Treatment of Heart Disease in Children*

Sol Robinson, Associate Clinical Professor of Pediatrics, Stanford University, School of Medicine, San Francisco, California

2.35 *P.M.—Re-Evaluation of the Medical Treatment of Hypertension*

William H. Thomas, Assistant Clinical Professor of Medicine, University of California, School of Medicine, San Francisco, California

3:10 *P.M.—The Recognition of Minor Myocardial Infarctions*

John J. Sampson, Clinical Professor of Medicine, University of California, School of Medicine, San Francisco, California

3:45 *P.M.—Vectorcardiography—Clinical and Research Applications*

Herman N. Uhley, Assistant in Medicine, Research Associate, Harold Brunn Institute, Mt. Zion Hospital, San Francisco, California

4:20 *P.M.—Recognition and Treatment of Cor Pulmonale*

Edward C. Rosenow, Jr., Associate Clinical Professor of Medicine, University of Southern California, School of Medicine, Los Angeles, California

A ten-minute question and answer period will follow each lecture

NOTE: These seminars on diseases of the chest will be presented at the Fairmont Hotel on Wednesday, June 18, and are open to all physicians. The seminars have been accredited by the Board of Examiners for candidates for Fellowship in the College. The registration fee for each seminar, which consists of a series of five lectures, is $7.50.

Registration for the seminars must be made in advance and accompanied by the tuition fee; seating capacity is limited and reservations will be accepted in the order received. A coupon for this purpose will be found on page 466. Please indicate your preference by number.

Please complete reservation form on page 466

SCIENTIFIC PROGRAM

Thursday, June 19

8:00 p.m.—Scientific Session

Chairmen:

Burgess L. Gordon, President, Albuquerque, New Mexico
Donald R. McKay, President-Elect, Buffalo, New York

THIRD LOUIS MARK MEMORIAL LECTURE

The Individual Man and Medicine
John B. deC. M. Saunders, Dean, School of Medicine; Professor of Anatomy and Chairman of the Department, University of California School of Medicine, San Francisco, California

PANEL ON THE JET AGE AND CHEST MEDICINE

Moderator:

W. Randolph Lovelace, II, Head, Section of Surgery, Lovelace Clinic, and Director, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

Panel:

Mr. Stanley Lippert, Coordinator, Human Factors Group, Interiors Design Section, Santa Monica Engineering Department, Douglas Aircraft Company, Inc., Santa Monica, California

Ulrich C. Luft, Head, Department of Physiology, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

David G. Simons, Major USAF, Chief, Space Biology Branch, Aero Medical Field Laboratory, Air Force Missile Development Center, Holoman Air Force Base, New Mexico

Kenneth L. Stratton, Director, Medical Services Division, American Airlines, LaGuardia Airport Station, New York

Clayton S. White, Director of Research, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

Friday, June 20

9:00 a.m.—Scientific Session No. 1

Opening Remarks:

Peter A. Theodos, Philadelphia, Pennsylvania, Chairman, Section on Pulmonary Diseases, Committee on Scientific Program

Symposium on Tuberculosis (Medical and Surgical)

Varieties of Acid Fast Bacilli and Their Relationship to Disease in Man
Emil Bogen, Director of Laboratories and Research, and Seymour Froman, Microbiologist, Olive View Sanatorium, Olive View, California

The Role of the Cycloserine (Seromycin) Blood Level in the Treatment of Pulmonary Tuberculosis and the Prevention and Control of Cycloserine (Seromycin) Toxicity
George E. Martin, Medical Director, K. I. Fetterhoff, and C. X. Holmes, Pittsburgh State Tuberculosis Hospital, Pittsburgh, Pennsylvania

Massive Dose Isoniazid Therapy in Chronic Pulmonary Tuberculosis
J. J. Kirschner, Medical Director, Eagleville Sanatorium, Eagleville, Penna.

Continued Observations on the Role of Steroid Therapy in Tuberculosis
Annabel B. Miller, Chief, Pulmonary Disease Section, Veterans Administration Hospital, Buffalo, New York

Success in Repeat Treatment vs. Original Treatment of Tuberculosis
W. L. Howard, Superintendent, W. H. Maybury Sanatorium, Northville, Mich.

A Study of Primary Tuberculosis with Emphasis on the Intradermal Tuberculin Reaction Before and After Treatment
William B. Leftwich, Chief, Pulmonary Disease Service, Highland Alameda County Hospital, Oakland, California

Specific Tuberculin Sensitivity
Lydia B. Edwards, Medical Director, Tuberculosis Program, Division of Special Health Services, Department of Health, Education and Welfare, Washington

Comparative Morbidity and Mortality of Antimicrobially Treated and Untreated Idiopathic Effusion in the Negro
John H. Seabury, Professor of Medicine, John B. Bobear, Instructor in Medicine and M. Jack Liberman, Louisiana State University School of Medicine, New Orleans, Louisiana

Friday, June 20 (continued)

The Management and Chemotherapy of Tuberculosis in Pregnancy
Irving J. Selikoff, and Henry L. Dorfmann, Department of Medicine (Thoracic Division), The Mount Sinai Hospital, New York City

Current Status of Surgery in Pulmonary Tuberculosis (A summary report)
Lyman A. Brewer, III, Associate Professor of Surgery, College of Medical Evangelists, and Edward L. King, Attending Staff, Los Angeles County Hospital, Los Angeles, California

9:00 a.m.—Scientific Session No. 2

Opening Remarks:
Samuel Bellet, Philadelphia, Pennsylvania, Chairman, Section on Cardiovascular Diseases, Committee on Scientific Program

Symposium on Clinical Cardiology

Some Factors in the Pathogenesis of Atherosclerosis
David M. Spain, Associate Professor of Pathology, Columbia University College of Physicians and Surgeons, New York City; and Victoria B. Bradess, Director, Department of Laboratories and Research, Westchester County, Valhalla, N. Y.

Angina Pectoris Inversa and Heberden's Angina; Clinical and Experimental Observations
Myron Prinzmetal, Professor of Clinical Medicine, University of California School of Medicine, Los Angeles, California; Naci Bor, Research Fellow, Takashi Wada, Research Fellow, and Rexford Kennamer, Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California

Factors in the Onset of Coronary Occlusion. Effort and Occupation
Arthur M. Master, Consultant Cardiologist, Mount Sinai Hospital, New York

The Clinical Use of Suprasternal Transaortic Coronary Arteriography
William Likoff, Associate Professor of Medicine, Joseph F. Uricchio, Associate in Medicine, William M. Lemmon, Resident in Thoracic Surgery and J. Stauffer Lehman, Professor and Head, Department of Radiology, Hahnemann Medical College, Philadelphia, Pennsylvania

Complete Relief of Mitral Stenosis by Neostrophingic Mobilization of the Obstructed Valve
Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Pulmonary Vascular Changes in Hypersensitivity States
George C. Griffith, Professor of Medicine (Cardiology), University of Southern California School of Medicine, Los Angeles, California

Chlorothiazide Therapy in Congestive Failure
Ralph V. Ford, Assistant Professor of Medicine and Pharmacology, Baylor University College of Medicine, Houston, Texas

12:00 noon—Round Table Luncheon Discussions (See page 454)

2:00 p.m.—Scientific Session No. 1

Forum on Basic Research in Diseases of the Chest: Pulmonary

Molar Sodium Lactate in Acute Adrenalin Fast Asthmatics
J. S. Blumenthal, Associate Clinical Professor of Medicine, E. B. Brown, Professor of Physiology, and G. S. Campbell, Assistant Professor of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

An Evaluation of an Improved Rapid Method of Measuring Oxygen Tension
William F. Miller, Assistant Professor of Medicine, Brian J. Sproule, Research Fellow and Ivan E. Cushing, Resident, Internal Medicine, University of Texas Southwestern Medical School and Parkland Memorial Hospital, Dallas, Texas

Experimental Silicosis: The Inhibitory Effect of Iron
Paul Gross, Research Pathologist, Marian L. Westrick, Research Toxicologist and James M. McNerney, Assistant Research Toxicologist, Industrial Hygiene Foundation of America, Inc., Mellon Institute, Pittsburgh, Pennsylvania

The Biological Action of Inhaled Submicron Amorphous Silica Dusts
G. W. H. Schepers, Institute of Industrial Health and Department of Pathology, University of Michigan, Ann Arbor, Michigan

Changes of Stores of Carbon Dioxide During Voluntary Hyperventilation
John W. Vance, Fellow in Medicine and Ward S. Fowler, Section on Physiology, Mayo Clinic and Foundation, Rochester, Minnesota

Friday, June 20 (continued)

Should A Chronic Atelectatic Lung Be Reaerated or Excised
John R. Benfield, Assistant Resident, Edwin T. Long, Resident Associate, Robert W. Harrison, Instructor, John F. Perkins, Jr., Associate Professor of Physiology, Gerald P. Herman, Intern, and William E. Adams, Raymond Professor of Surgery, University of Chicago School of Medicine, Chicago, Illinois

Fluoroscopic Pulmonary Densiography: Application to the Diagnosis of Chest Disease
Albert H. Andrews, Jr., Attending Bronchoesophagologist and Director, Respiration Laboratory, Robert J. Jensik, Attending Thoracic Surgeon, and William H. Pfisterer, Attending Radiologist, Presbyterian-St. Luke's Hospital, Chicago

Effect of Intermittent Positive Pressure Breathing on the Cardiac Output
Richard T. Cathcart, Assistant Professor of Medicine, William Fraimow, Fellow in Cardiopulmonary Research, Thomas Nealon, Instructor in Surgery, and Joyce Price, R.N., Jefferson Medical College, Philadelphia, Pennsylvania

2:00 *p.m.—Scientific Session No. 2*

Forum on Basic Research in Diseases of the Chest: Cardiac

Measurement of Thoracic Lymphatic Flow in Dogs by a New Method, With Its Clinical Implications
Herman N. Uhley, Assistant in Medicine, Sanford E. Leeds, Associate Chief of Surgery, John J. Sampson, Chief of Medicine, Mount Zion Hospital, and Meyer Friedman, Director, Harold Brunn Institute, Mount Zion Hospital, San Francisco, California

Newer Aspects of Diagnostic and Therapeutic Management of Acute Idiopathic Pericarditis
R. E. Fremont, Clinical Assistant Professor of Medicine, State University of New York Downstate Medical Center, Brooklyn, New York

Determinants of Pulmonary Blood Volume and Vascular Pressures
Peter F. Salisbury, Institute for Medical Research and Department of Medicine and Pierre-M. Galletti, Research Fellow, Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California

Myocardial Revascularization by Cardiopneumopexy (185 Dogs and 21 Humans)
Franklin R. Smith, Clinical Associate in Surgery, University of Washington School of Medicine, Seattle, Washington

Left Heart Catheterization for the Evaluation of Mitral and Aortic Valvular Disease
William S. Blakemore, J. William White Assistant Professor of Surgical Research, Harrison Department of Surgical Research, H. M. Woske, Associate in Medicine, D. F. Heiman, Instructor in Medicine, B. Jumbala, Instructor in Medicine and Hadley Conn, Assistant Professor of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Hemodynamic Response of Brain, Liver, Kidney and Coronary Circulation to Vasopressor Drugs
Eliot Corday, Assistant Clinical Professor of Medicine, John Williams, Research Fellow, Lauro B. de Vera, Research Fellow and Herbert Gold, Instructor in Medicine, University of California School of Medicine, Los Angeles, California

The Use of Extracorporeal Circulation in Cardiac Surgery
F. Henry Ellis, Jr., Head of a Surgical Section, and John W. Kirklin, Head of a Surgical Section, Mayo Clinic, Rochester, Minnesota

8:15 *p.m.—Scientific Session*

"Fireside Conferences"
Subjects and Discussion Leaders

Management of Pulmonary Emphysema
Alvan L. Barach, Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York City
Ward S. Fowler, Consultant in Physiology, Mayo Clinic, Rochester, Minnesota

Cancer of the Lung
L. Henry Garland, Clinical Professor of Radiology, Stanford University School of Medicine, San Francisco, California
Robert R. Shaw, Clinical Professor of Surgery, University of Texas Southwestern Medical School, Dallas, Texas

Fireside Conferences (continued)

Risk of Major Surgery in Cardiac Operation and Results of Aortic and Mitral Valve Surgery. Recent Advances

W. Donald Close, Associate Professor of Medicine, Indiana University School of Medicine, Indianapolis, Indiana
C. Walton Lillehei, Professor of Surgery, University of Minnesota Medical School and Variety Club Heart Hospital, Minneapolis, Minnesota

Electrocardiography. Vectorcardiography. Ballistocardiography.

George E. Burch, Henderson Professor and Chairman, Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana
Manuel Gardberg, Clinical Associate Professor of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana

Recent Developments in Tuberculin Testing

J. Arthur Myers, Professor of Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Minneapolis, Minnesota
Julius B. Novak, Medical Director, Tuberculosis Institute of Chicago, Illinois

The Viruses in Respiratory Diseases

Milton V. Davis, Thoracic Surgeon, Dallas, Texas
Edwin H. Lennette, Chief, Viral and Rickettsial Disease Laboratory, California State Department of Public Health, Berkeley, California
Thomas G. Ward, Professor of Virology, University of Notre Dame, Notre Dame, Indiana

Anticoagulant Therapy

Lawrence R. Coke, Assistant Professor of Medicine, University of Manitoba, Winnipeg, Manitoba
Benjamin Manchester, Assistant Clinical Professor of Medicine, George Washington University School of Medicine, Washington, D. C.

Immunization in Tuberculosis

Lewis S. Jordan, Superintendent and Medical Director, Riverside Sanatorium, Granite Falls, Minnesota
Sol Roy Rosenthal, Medical Director, Research Foundation, Chicago, Illinois

Esophageal Disease

Roy G. Klepser, Associate Professor of Thoracic Surgery, Georgetown University Medical School, Washington, D. C.
Herman J. Moersch, Chairman, Section of Internal Medicine, Mayo Clinic, Rochester, Minnesota
Elmer C. Rigby, Active Staff, St. Vincent's Hospital, Los Angeles, California

Cor Pulmonale

George R. Herrmann, Professor of Medicine, University of Texas Medical Branch, Galveston, Texas
Irving Mack, Associate Attending Physician, Chest Department, Michael Reese Hospital, Chicago, Illinois

The Use of Inhalation Therapy

Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago, Illinois
Theodore H. Noehren, Assistant Professor of Internal Medicine, University of Buffalo College of Medicine and the Buffalo General Hospital, Buffalo, New York
Max S. Sadove, Division of Anesthesiology, University of Illinois Research and Educational Hospitals, Chicago, Illinois

The Chest Physician in Court

Mr. Edward D. Bronson, Attorney-at-law, San Francisco, California
Mr. John Wynne Herron, Trial Attorney, San Francisco, California
Joseph F. Sadusk, Jr., Member, Committee on Medico-Legal Problems, American Medical Association; Associate Clinical Professor of Medicine, Stanford University School of Medicine, San Francisco, California

Coronary Disease Including Medical and Surgical Therapy

B. L. Brofman, Director, Cardiovascular Research, Mount Sinai Hospital, Cleveland, Ohio
Johann L. Ehrenhaft, Professor of Surgery, Chairman, Division of Thoracic Surgery, State University of Iowa, Iowa City, Iowa
Joseph Edeiken, Assistant Professor of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Pulmonary Aspects of Collagen Diseases

Benson Bloom, Assistant Director of Professional Services, Veterans Administration Hospital, Bronx, N. Y.
O. J. Farness, Private practice, Diseases of the Chest, Tucson, Arizona

Fireside Conferences (continued)

Fungus Diseases of the Chest
Michael L. Furcolow, Medical Director, Public Health Service, Kansas City, Kans.
B. H. Webster, Visiting Physician, Department of Chest and Internal Medicine, St. Thomas Hospital, Nashville, Tennessee

Rheumatic and Congenital Heart Disease—Therapy and Prophylaxis
Benjamin M. Gasul, Director, Pediatric Cardiophysiology Department, Cook County Children's Hospital, Chicago, Illinois
Richard D. Rowe, Assistant Physician, Hospital for Sick Children, Toronto

The Practical Evaluation of Lung Function
S. Thatcher Hubbard, Jr., Director, Cardio-Respiratory Laboratory (Private), Spokane, Washington
Ross C. Kory, Associate Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

Sarcoidosis
Martin M. Cummings, Director, Research Service, Veterans Administration, Washington, D. C.
Edward Lebovitz, Instructor of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
David Salkin, Director, Professional Services, Veterans Administration Hospital, San Fernando, California

Resuscitation of Heart—Treatment of Cardiac Arrest
Thomas G. Baffes, Assistant Attending Surgeon, Children's Memorial Hospital, Chicago, Illinois
E. Sterling Nichol, formerly Medical Director, Miami Heart Institute, Miami Beach, Florida
J. Karl Poppe, Clinical Associate, Department of Surgery, University of Oregon Medical School, Portland, Oregon

The Use and Abuse of Steroid Therapy in Pulmonary Disease
Winthrop N. Davey, Associate Professor in Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan
David B. Radner, Director, Chest Department, Michael Reese Hospital, Chicago

Biopsy Procedures in Chest Diseases
Albert C. Daniels, Clinical Assistant Professor of Surgery, Stanford University School of Medicine, San Francisco, California
Karl P. Klassen, Chief of the Thoracic Surgery Service, Ohio State University Health Center, Columbus, Ohio

Hypertension
Thomas J. Coogan, Associate in Medicine, University of Illinois College of Medicine, Chicago, Illinois
Milton Mendlowitz, Associate Attending Physician, Mount Sinai Hospital, New York City

Allergy in Pulmonary Disease
Leon Unger, Associate Professor of Medicine, Northwestern University Medical School, Chicago, Illinois
Orval R. Withers, Associate Clinical Professor of Medicine, University of Kansas School of Medicine, Kansas City, Missouri

Arrhythmias
Louis F. Bishop, Assistant Clinical Professor of Medicine, New York University College of Medicine, New York City
Arthur E. Lamb, Clinical Associate Professor of Medicine, State University of New York College of Medicine, New York City

Management of Chest Injuries
David P. Boyd, Thoracic Surgeon, Lahey Clinic, Boston, Massachusetts
Emil A. Naclerio, Chief, Thoracic Surgery, Harlem Hospital, New York

Treatment of Tuberculosis in Infants and Children
Lloyd B. Dickey, Professor of Pediatrics, Stanford University School of Medicine, San Francisco, California
Katherine H. K. Hsu, Assistant Professor of Pediatrics, Baylor University College of Medicine, Houston, Texas

Trauma in Heart Disease. Medico-Legal Aspects of Cardiovascular Disease
Mr. Edmund J. Thomas, Secretary-Presiding Referee, Industrial Accident Commission, San Francisco, California
Henry J. Stanford, Consultant Thoracic Surgeon, Veterans Administration Hospital, Tucson, Arizona

Fireside Conferences (continued)

New Trends in Physical Rehabilitation of Cardio-Pulmonary Disease
John H. Aldes, Director, Rehabilitation Center, Cedars of Lebanon Hospital, Los Angeles, California
Edward A. Piszczek, Field Director, The Suburban Cook County Tuberculosis Sanitarium District, Forest Park, Illinois

Saturday, June 21

10:00 a.m.—Combined Scientific Session

Pulmonary and Cardiac Function Studies in Sickle Cell Lung Disease
Kenneth M. Moser, Assistant Chief, Peter C. Luchsinger, Chief, Cardiopulmonary Laboratory, District of Columbia General Hospital, Washington, D. C., and Sol Katz, Adjunct Clinical Professor of Medicine, Georgetown and George Washington University Medical Schools, Washington, D. C.

Bronchogenic Cysts in Patients Presumed to Have Pulmonary Tuberculosis
Neil C. Andrews, Chief of Surgery, Philip C. Pratt, Chief of Laboratories and A. J. Christoforidis, Chief of Radiology, Ohio Tuberculosis Hospital, Columbus, Ohio

Forum on Pulmonary and Cardiovascular Effects of Smoking

Moderator:
Julius H. Comroe, Director, Cardiovascular Research Institute, University of California Medical Center, San Francisco, California

Panel:
Kelly T. McKee, Associate Professor of Medicine, Medical College of South Carolina, Charleston, South Carolina
McKeen Cattell, Professor of Clinical Pharmacology, Cornell University Medical College, New York City
Richard J. Bing, Professor of Medicine, Washington University School of Medicine, St. Louis, Missouri

12:00 noon—Round Table Luncheon Discussions (See page 455)

2:00 p.m.—Scientific Session No. 1

Implications of Recent Findings on the Pathology and Pathogenesis of Benign Pulmonary Histoplasmosis
Henry C. Sweany, Director of Research and Pathology, David F. Gorelick, Consulting Pathologist, Fred C. Coller, Consulting Pathologist and James L. Jones, Histological Technician, Missouri State Sanatorium, Mount Vernon, Missouri

Middle Lobe Disease
David H. Waterman, Sheldon E. Domm and William K. Rogers, Attending Thoracic Surgeons, University of Tennessee Memorial Research Center and Hospital, Knoxville, Tennessee

Trigger Mechanisms in Asthma
Richard H. Overholt, Thoracic Surgeon, New England Deaconess and New England Baptist Hospitals, Boston, Massachusetts

Symposium on Idiopathic Interstitial Fibrosis of the Lung

Moderator:
H. Corwin Hinshaw, Clinical Professor of Medicine (Diseases of the Chest), Stanford University School of Medicine, San Francisco, California

Panel:
Hurley L. Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California, Los Angeles, California
David M. Spain, Associate Professor of Pathology, Columbia University College of Physicians and Surgeons, New York City
Gary Zucker, Assistant Clinical Professor of Medicine, New York University College of Medicine, New York City

2:00 p.m.—Scientific Session No. 2

Coronary Arteriography
Charles T. Dotter, Professor of Radiology, Louis H. Frische, Associate Professor of Radiology, Etsuko Kawashima, Resident in Radiology, and W. Hoskinson, Medical Student, University of Oregon Medical School, Portland, Oregon

Intracardiac Surgery Using the Kay-Anderson Heart Lung Machine
Jerome Harold Kay, Robert M. Anderson, Louis C. Bennett, Rubin Lewis, William Musicant, Edward M. Synder, Jr., John Meihaus, Oscar Magidson and Jack Sheinkopf, University of Southern California School of Medicine and St. Vincent's Hospital, Los Angeles, California

Saturday, June 21 (continued)

The Use of Myocardial Electrode Inserted Percutaneously for Control of Complete Atrial Ventricular Block by an Artificial Pacemaker
C. Walton Lillehei, Professor of Surgery, Andre Thenet and Paul Hodges, University of Minnesota Medical School and Variety Club Heart Hospital, Minneapolis, Minnesota

Surgery in Mitral Stenosis—(The report of the Section on Cardiovascular Surgery of the Committee on Cardiovascular Disease)
Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Panel on Atherosclerosis

Moderator:
William Likoff, Associate Professor of Medicine, Hahnemann Medical College, Philadelphia, Pennsylvania

Panel:
George E. Burch, Henderson Professor and Chairman, Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana
Stephen R. Elek, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California
Maurice Sokolow, Associate Professor of Medicine, Chief of Cardiovascular Division, Department of Medicine, University of California School of Medicine, San Francisco, California

Sunday, June 22

9:00 a.m.—Scientific Session No. 1

Symposium on the Biologic Effects of Radio-Active Exposure on the Lungs

Moderator:
L. Henry Garland, Clinical Professor of Radiology, Stanford University School of Medicine, San Francisco, California

Panel:
Hardin B. Jones, Professor of Physiology, University of California School of Medicine, San Francisco, California
George R. Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee
Sydney F. Thomas, Assistant Clinical Professor of Radiology, Stanford University School of Medicine, San Francisco, California

Symposium on the Biologic Effects of Air Pollution on the Lungs

Moderator:
Seymour M. Farber, Associate Clinical Professor of Medicine, In Charge, University of California Tuberculosis and Chest Service, San Francisco, California

Panel:
John R. Goldsmith, Head, Studies of Health Effects of Air Pollution, California Department of Public Health, Berkeley, California
Albert Roberts, Chief, Clinical Investigation, Air Pollution Medical Program, Public Health Service, Wahsington, D. C.
Moyer D. Thomas (D.Sc.), Stanford Research Institute, Menlo Park, Cal.

9:00 a.m.—Scientific Session No. 2

Clinical Cardiac Conference

Moderator:
John J. Sampson, Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Panel:
Jesse L. Carr, Clinical Professor of Pathology, University of California School of Medicine, San Francisco, California
Eliot Corday, Assistant Clinical Professor of Medicine, University of California School of Medicine, Los Angeles, California
Earle B. Kay, Director of Cardiovascular Surgery, St. Vincent's Charity Hospital, Cleveland, Ohio
Arthur M. Master, Consultant Cardiologist, The Mount Sinai Hospital, New York City
Arthur Selzer, Clinical Professor of Medicine, Stanford University School of Medicine, San Francisco, California

Sunday, June 22 (continued)

Symposium on Congenital Heart Disease

Moderator:

Saul J. Robinson, Associate Clinical Professor of Pediatrics, Stanford University School of Medicine, Chief of Pediatrics, Mount Zion Hospital, San Francisco, California

The Pathologic Anatomy of Ventricular Septal Defects
Maurice Lev, Director, Congenital Heart Disease Research and Training Center, Hektoen Institute, Chicago, Illinois

Follow-Up Studies on the Hemodynamics of Ventricular Septal Defects
Joshua Lynfield, Associate in Cardiophysiology, Cook County Hospital, Chicago, Illinois

Clinical Findings in Patients with Ventricular Septal Defects
James DuShane, Assistant Professor of Pediatrics, University of Minnesota Graduate School of Medicine, Rochester, Minnesota

Present Day Views Regarding Surgery in Patients with Ventricular Septal Defects
Denton A. Cooley, Associate Professor of Surgery, and Dan G. McNamara, Associate Professor of Pediatrics, Baylor University College of Medicine, Houston, Texas

PANEL DISCUSSION

Moderator:

Saul J. Robinson, San Francisco, California

Panel:

Denton A. Cooley, Houston, Texas
James DuShane, Rochester, Minnesota
Maurice Lev, Chicago, Illinois
Joshua Lynfield, Chicago, Illinois

12:00 noon—Round Table Luncheon Discussions *(See page 456)*

2:00 p.m.—Combined Scientific Session

Clinical and Roentgenologic Signs of Collagen Diseases Involving the Thorax
Charles M. Nice, Jr., Associate Professor of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota; A. N. K. Menon, Lecturer in Radiology, Stanley Medical College, Madras, India, and Leo G. Rigler, Director of Postgraduate Medical Education, Cedars of Lebanon Hospital, Los Angeles, California

Myasthenia and Malignant Intrathoracic Tumors
Edward H. Lambert, Associate Professor of Physiology, E. Douglas Rooke, Instructor in Neurology, Lee M. Eaton, Professor of Neurology, and Corrin H. Hodgson, Assistant Professor of Medicine, Mayo Foundation Graduate School, University of Minnesota, Minneapolis, Minnesota

Primary Pulmonary Hypertension
Harry Goldberg, Assistant Professor of Medicine, Jonas Brachfeld, Former Cardiac Fellow, and Attilio Reale, Former Cardiac Fellow, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

The Prognosis of Lung Cancer
Katharine R. Boucot, Professor of Preventive Medicine and Clinical Professor of Medicine, Utako Horie, Lois Mattox Miller Fellow in Preventive Medicine, Woman's Medical College of Pennsylvania; and Martin J. Sokoloff, Associate Professor of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

Evolution of Carcinoma of the Lung
Leo G. Rigler, Director of Postgraduate Medical Education, Cedars of Lebanon Hospital, Los Angeles, California

Post Traumatic Aneurysm of the Thoracic Aorta
James C. Hunt, Section of Medicine, Howard B. Burchell, and F. Henry Ellis, Section of Surgery, Mayo Clinic, Rochester, Minnesota

Esophageal Replacement with a Reversed Gastric Tube
Henry J. Heimlich, Adjunct Thoracic Surgeon, Montefiore Hospital, New York City

Intracardiac Anatomy in Patients with Congenital Heart Lesions
F. Mason Sones, Jr., Director, Cardiac Catheterization Laboratory, Cleveland Clinic Foundation, Cleveland, Ohio

ROUND TABLE LUNCHEONS

Friday, June 20

A-1 ***Recent Advances in Diagnosis and Therapy of Coronary Disease***

Richard A. Gilman, Thoracic and Cardiovascular Surgeon, San Diego, California

Lewis Gunther, Co-Chief of Medicine, Cedars of Lebanon Hospital, Los Angeles, California

Nathaniel E. Reich, Clinical Assistant Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

Moderator: **Oglesby Paul**, Clinical Associate Professor of Medicine, University of Illinois College of Medicine, Chief of Cardiac Clinic and Assistant Attending Physician, Presbyterian Hospital, Chicago, Illinois

A-2 ***Cardiac in Industry***

Daniel C. Braun, Lecturer in Occupational Medicine, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania

Samuel A. Weisman, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

Paul J. Whitaker, Medical Director, Allis-Chalmers Manufacturing Company, West Allis, Wisconsin

Moderator: **John F. Briggs**, Associate Professor of Clinical Medicine, University of Minnesota, Minneapolis, Minnesota

A-3 ***Treatment of the Patient with Inoperable Lung Cancer***

William F. Mazzitello, Assistant Professor of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

John P. Medelman, Clinical Associate Professor of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota

Richard H. Overholt, Thoracic Surgeon, New England Deaconess Hospital, Boston, Massachusetts

Moderator: **William E. Adams**, Raymond Professor of Surgery, University of Chicago School of Medicine, Chicago, Illinois

A-4 ***Management of Chronic Respiratory Insufficiency***

Howard G. Dayman, Assistant Professor of Medicine, University of Buffalo School of Medicine, Buffalo, New York

Marvin S. Harris, Clinical Professor of Thoracic Diseases, College of Medical Evangelists, Los Angeles, California

William Lees, Chief of Surgery, Municipal Tuberculosis Sanatorium, Associate Clinical Professor in Surgery, Stritch School of Medicine of Loyola University, Chicago, Illinois

Moderator: **Maurice S. Segal**, Clinical Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts

A-5 ***Management of the Tuberculous Patient Unresponsive to the Usual Methods of Treatment***

Sumner S. Cohen, Assistant Medical Director, Glen Lake Sanatorium, Oak Terrace, Minnesota

Roger S. Mitchell, Associate Professor of Medicine, University of Colorado School of Medicine, Denver, Colorado

James A. Wier, Col., Chief, Pulmonary Disease Service, Fitzsimons Army Hospital, Denver, Colorado

Moderator: **Karl H. Pfuetze**, Medical Director and Superintendent, Chicago State Tuberculosis Sanatorium, Chicago, Illinois

A-6 ***Newer Antibiotic Therapy of Non-Tuberculous Infections of the Respiratory Tract***

Joseph E. Geraci, Assistant Professor of Medicine, Mayo Clinic and University of Minnesota Graduate School of Medicine, Rochester, Minnesota

Alfred Goldman, Associate Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Missouri

William M. M. Kirby, Professor of Medicine, University of Washington Medical School, Seattle, Washington

Moderator: **Robert I. Wise**, Assistant Professor of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

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ROUND TABLE LUNCHEONS

Saturday, June 21

B-1 ***Selection of Patients for Surgery with Acquired Valvular Lesions***

Robert P. Glover, Director of Cardiovascular Research Laboratories and Chief of Thoracic and Cardiac Surgery, Presbyterian Hospital, Philadelphia, Pennsylvania

Alfred Goldman, Director, Cardiac Hospital, City of Hope Medical Center, Duarte, California

Henry A. Zimmerman, Chief of Cardiovascular Service, St. Vincent's Charity Hospital, Cleveland, Ohio

Moderator: **Arthur Selzer**, Clinical Professor of Medicine, Stanford University School of Medicine, San Francisco, California

B-2 ***Trauma and Heart Disease (Rehabilitation)***

Ray W. Kissane, Professor of Medicine in Cardiology, Ohio State University College of Medicine, Columbus, Ohio

H. Easton McMahon, Assistant Clinical Professor of Medicine, New York Medical College, New York City

Joseph M. Ryan, Clinical Assistant Professor of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

Moderator: **Philip Lee**, Department of Medicine, Palo Alto Medical Clinic, Palo Alto, California

B-3 ***Present Indications for Thoracic Surgical Procedures***

E. C. Drash, Clinical Professor of Surgery, University of Virginia School of Medicine, Charlottesville, Virginia

John B. Grow, Chief, Thoracic Surgery, National Jewish Hospital, Denver, Colorado

W. Elliott Harrison, Clinical Assistant Professor of Surgery, University of British Columbia, Vancouver, British Columbia

Moderator: **Paul C. Samson**, Associate Clinical Professor of Surgery, Stanford University School of Medicine, San Francisco, California

B-4 ***Pulmonary Embolism***

Chilton Crane, Senior Associate in Surgery, Peter Bent Brigham Hospital, Boston, Massachusetts

Ivan F. Duff, Associate Professor of Internal Medicine in Charge of Rackham Arthritis Research Unit, University of Michigan, Ann Arbor, Michigan

Travis Winsor, Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

Moderator: **Harold L. Israel**, Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

B-5 ***Problems in the Early Diagnosis of Pulmonary Emphysema***

J. K. Curtis, Clinical Professor of Medicine, University of Wisconsin Medical School, Madison, Wisconsin

Harold A. Lyons, Associate Professor of Medicine, State University of New York, Downstate Medical Center, Brooklyn, New York

Bernard J. O'Loughlin, Associate Professor of Radiology, University of California School of Medicine, Los Angeles, California

Moderator: **R. Drew Miller**, Assistant Professor of Medicine, University of Minnesota Graduate Medical School, Rochester, Minnesota

B-6 ***The Evaluation of Disability in Industrial Lung Diseases***

Mr. Warren L. Hanna, Attorney-at-law, San Francisco, California

Abraham H. Russakoff, Associate Clinical Professor of Medicine, Medical College of Alabama, Birmingham, Alabama

Joseph F. Tomashefski, Assistant Professor of Medicine and Physiology, Ohio State University College of Medicine, Columbus, Ohio

Mr. Theodore C. Waters, Attorney-at-law, Baltimore, Maryland

Moderator: **Reginald H. Smart**, Clinical Professor of Medicine and Coordinator of Chest Disease Instruction, University of Southern California School of Medicine, Los Angeles, California

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ROUND TABLE LUNCHEONS

Sunday, June 22

C-1 ***Recent Advances in Cardiac Therapy***

Milton W. Anderson, Consultant in Medicine, Mayo Clinic, Rochester, Minnesota

John M. Askey, Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

Benjamin Manchester, Assistant Clinical Professor of Medicine, George Washington University School of Medicine, Washington, D. C.

Moderator: **John J. Sampson**, Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

C-2 ***Congenital Malformations of the Heart***

Paul Adams, Jr., Assistant Professor of Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota

Robert A. Miller, Head Cardiologist, Children's Memorial Hospital, Chicago, Illinois

Morse Shapiro, Senior Cardiac Consultant, City of Hope Medical Center, Duarte, California

Moderator: **Forrest Adams**, Associate Professor of Pediatrics (Cardiology) University of California School of Medicine, Los Angeles, California

C-3 ***Problems in the Selection of Patients for Travel by Air—Present and Future***

Earl T. Carter, Assistant Professor of Preventive Medicine and Physiology, Ohio State University College of Medicine, Columbus, Ohio

Ross C. Kory, Associate Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

Ludwig G. Lederer, Chairman, Medical Committee, Air Transport Association of America, Washington, D. C.

Moderator: **Roger H. L. Wilson**, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

C-4 ***Physiologic Treatment of Pulmonary Disease in Children***

John E. Affeldt, Medical Director, Rancho Los Amigos Respiratory Center for Polio, Hondo, California

Gordon E. Gibbs, Professor and Chairman, Department of Pediatrics, University of Nebraska College of Medicine, Omaha, Nebraska

Allan Hurst, Assistant Professor of Medicine, University of Colorado School of Medicine, Denver, Colorado

Moderator: **Roy F. Goddard**, Director, Pediatric Research Department, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

C-5 ***Pulmonary Manifestations of Cardiac Disease***

Arnold S. Anderson, Private practice, Diseases of the Chest, St. Petersburg, Florida

John S. LaDue, Associate Professor of Medicine, Cornell University Medical College, New York City

Paul C. Swenson, formerly Professor of Radiology, Jefferson Medical College, Philadelphia, Pennsylvania

Moderator: **Corrin H. Hodgson**, Consultant in Internal Medicine, Mayo Clinic, Rochester, Minnesota

C-6 ***The Management of Pulmonary Disease in Geriatric Patients***

Duane M. Carr, Professor of Surgery, University of Tennessee College of Medicine, Memphis, Tennessee

Alexander Libow, Associate Attending, Mount Sinai Hospital, Miami Beach, Florida

Joseph A. Smith, Medical Director, New Jersey Sanatorium for Chest Diseases, Glen Gardner, New Jersey

Moderator: **Edward Kupka**, Chief, Bureau of Tuberculosis, California State Department of Public Health, Berkeley, California

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SPECIAL EVENTS

Wednesday, June 18

3:30 p.m.—SEMINAR, COUNCIL AND COMMITTEE ON UNDERGRADUATE MEDICAL EDUCATION

Undergraduate Teaching of Tuberculosis and Chest Diseases at the University of California School of Medicine

Moderator: Seymour M. Farber, In Charge, University of California Tuberculosis and Chest Service, San Francisco, California

Differential Diagnosis

Alvin S. Hambly, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Antimicrobial Therapy

William Mandel, Clinical Instructor in Medicine, University of California School of Medicine, San Francisco, California

Pulmonary Physiology

Roger H. L. Wilson, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Cancer Cytology

Sam Pfarr, Senior Cytology Technician, University of California School of Medicine, San Francisco, California

Thoracic Surgery

Max E. Childress, Clinical Instructor in Surgery, University of California School of Medicine, San Francisco, California

Summarization

Mortimer A. Benioff, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Discussion

Theodore H. Noehren, Buffalo, New York
Chairman, Council on Undergraduate Medical Education

William M. Lees, Chicago, Illinois
Chairman, Committee on Undergraduate Medical Education

Thursday, June 19

4:00 p.m.—OPEN FORUM, COUNCIL ON HOSPITALS

Have We Exhausted Our Case-Finding in Chest Disease?

Chairman: Otto L. Bettag, Director, Illinois Department of Public Welfare, Chicago

Communities

Edward T. Blomquist, Medical Director, Chief, Tuberculosis Program, Division of Special Health Services, Department of Health, Education, and Welfare, Public Health Service, Washington, D. C.

Penal Institutions

John H. Fountain, Director, Division of Tuberculosis Control, King County Health Department, Seattle, Washington

General Hospitals

John P. Medelman, Clinical Associate Professor of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota

Schools

J. Arthur Myers, Professor of Internal Medicine and Public Health, Medical and Graduate Schools, University of Minnesota, Minneapolis, Minnesota

Mental Institutions

Ernest Teller, Chief, Tuberculosis Control Service, Illinois Department of Public Welfare, Chicago, Illinois

Questions and discussion from the floor

4:00 p.m.—OPEN FORUM, COUNCIL ON RESEARCH

Alvan L. Barach, New York City, Chairman, Council on Research, presiding

Presentation of Committee Reports

The above meetings are open to all members of the College. Discussion from the floor.

ADMINISTRATIVE SESSIONS

Wednesday, June 18

8:00 a.m.—Committee on Seminars

10:00 a.m.—Executive Council

2:00 p.m.—Board of Regents

Thursday, June 19

9:00 a.m.—Meetings of all Councils and Committees

9:00 a.m.—Examinations for Fellowship (written)

12:00 noon—LUNCHEON, JOINT MEETING

Board of Governors and Boards of Regents

David H. Waterman, Knoxville, Tennessee, Chairman, Board of Governors, presiding

Awarding of Certificates of Merit to Past-Presidents of College Chapters

Burgess L. Gordon, Albuquerque, New Mexico, President

Presentation of Reports

Council on Undergraduate Medical Education
Theodore H. Noehren, Buffalo, New York, Chairman

Council on Postgraduate Medical Education
J. Winthrop Peabody Sr., Washington, D. C., Chairman

Council on Research
Alvan L. Barach, New York, N. Y., Chairman

Council on Hospitals
Otto L. Bettag, Chicago, Illinois, Chairman

Committee on Membership
Chevalier L. Jackson, Philadelphia, Pennsylvania, Chairman

Committee on Motion Pictures
Paul H. Holinger, Chicago, Illinois, Chairman

Committee on Liaison with State and County Medical Societies
Robert B. Morrison, Austin, Texas, Chairman

Committee on College Essay Contest
H. Allan Novack, Boston, Massachusetts, Chairman

College Books
Burgess L. Gordon, Albuquerque, New Mexico

Fifth International Congress on Diseases of the Chest
Tokyo, Japan, September 7-11, 1958
Murray Kornfeld, Chicago, Illinois

Silver Anniversary, 25th Annual Meeting
Atlantic City, June 3-7, 1959
Jay Arthur Myers, Minneapolis, Minnesota

Silver Anniversary, Homecoming Meeting
Albuquerque, New Mexico, 1959
Roy F. Goddard, Albuquerque, New Mexico

Silver Anniversary, Interim Session
Dallas, Texas, November 29-30, 1959
Alvis E. Greer, Houston, Texas

1:30 p.m.—Meeting, Oral Examiners

2:00 p.m.—Examinations for Fellowship (oral)

2:00 p.m.—Meetings of Council and Committee Chairmen

2:30 p.m.—Joint Meeting, Committee on Membership and College Chapter Officials

Friday, June 20

2:00 p.m.—Committee on Nominations

2:00 p.m.—Committee on Insurance

3:00 p.m.—Editorial Board

5:00 p.m.—Chapter Meetings

Saturday, June 21

9:00 a.m.—OPEN ADMINISTRATIVE SESSION
Burgess L. Gordon, Albuquerque, New Mexico, President, presiding
Report of the Historian
Report of the Treasurer
Report of the Executive Director
Report of the Committee on Nominations
Election of Officers

10:00 a.m.—Executive Council

Sunday, June 22

8:00 a.m.—Past-Presidents' Breakfast

10:00 a.m.—Executive Council

2:30 p.m.—Board of Regents

5:00 p.m.—Dinner Meeting, Section on Pediatric Cardiology
Benjamin M. Gasul, Chicago, Illinois, Chairman, presiding

SOCIAL ACTIVITIES

Saturday, June 21

6:00 p.m.—Annual Convocation (Formal)

7:00 p.m.—Cocktail Party
Sponsored by The Panray Corp., New York City

7:30 p.m.—Annual Presidents' Banquet
This is strictly a social evening and there will be no speeches

9:30 p.m.—After-Dinner Dancing
Sponsored by the California Chapter of the College. Music by the Jimmy Blass Orchestra

The above functions will be held at the Fairmont Hotel

LADIES ACTIVITIES

Thursday, June 19

12:30 p.m.—Luncheon, Piro's Restaurant
Within pleasant walking distance of delightful Jackson Square in one of the oldest sections of San Francisco. The Interior Decorator Display Shops will have open house with conducted tours especially for the ladies of the College.

Friday, June 20

6:30 p.m.—Cocktails

7:00 p.m.—Oriental Dinner, Terrace Room, Fairmont Hotel
Dinner will be followed by a Japanese Fashion Show including an enticing combination of costumes designed for modern leisure wear in Japanese fabrics and authentic Japanese Kimonos.

Saturday, June 21

6:00 p.m.—College Convocation

7:00 p.m.—Cocktail Party
Sponsored by The Panray Corp., New York City

7:30 p.m.—Annual Presidents' Banquet
This is a social event — no speeches

9:30 p.m.—After-Dinner Dancing
Sponsored by the California Chapter of the College. Music by the Jimmy Blass Orchestra

The Saturday functions will be held at the Fairmont Hotel

Sunday, June 22

Information brochures will be available at the Ladies Registration Desk and the members of the Ladies Reception Committee will be pleased to assist in arrangements for shopping, tours of Chinatown, Fisherman's Wharf, and other places of interest.

MOTION PICTURE PROGRAM

The following is a tentative program of films dealing with diseases of the chest which will be shown concurrently with the scientific program on Friday, Saturday and Sunday, June 20, 21 and 22. Additional films are being considered by the Committee on Motion Pictures of the College for presentation.

Differential Diagnosis and Treatment of Lobar Emphysema of Infants

Osler A. Abbott, Emory University School of Medicine, Emory University, Georgia

Traumatic Hernia of the Diaphragm

William E. Adams, John Todd Reynolds and Peter V. Moulder, University of Chicago and University of Illinois, Chicago, Illinois

Transposition of the Great Vessels

Thomas G. Baffes and Willis J. Potts, Children's Memorial Hospital, Chicago, Ill.

Segmental Resections of Multiple Congenital Arteriovenous Aneurysms

O. Theron Clagett, Mayo Clinic, Rochester, Minnesota

Surgical Removal Myxoma Left Auricle Simulating Mitral Stenosis

Denton A. Cooley and Joseph R. Latson, Baylor University College of Medicine, Houston, Texas

Repair of Interatrial Septal Defect Utilizing Cardiopulmonary By-Pass

Philip Crastnopol, Alvin A. Bakst, H. Gianfrancesco, E. A. Braunstein and Irving G. Kroop, Jewish Hospital and Jewish Chronic Disease Hospital, Brooklyn, New York

Closure of Interventricular Septal Defect Using the Pump Oxygenator

J. L. Ehrenhaft, State University of Iowa Hospitals, Iowa City, Iowa

Surgical Management of the Complications of Reflux Esophagitis

F. Henry Ellis, Jr., Mayo Clinic, Rochester, Minnesota

Esophageal Reconstruction with Colon Transplant

Paul F. Fox and David S. Jones, Stritch School of Medicine, Loyola University, Chicago, Illinois

The Mitral Valve—Dynamic Pathology and Surgery

Robert P. Glover, Julio C. Davila and Robert G. Trout, The Presbyterian Hospital, Philadelphia, Pennsylvania

Esophageal Replacement by a Reversed Gastric Tube

Henry J. Heimlich, New Rochelle, New York

Cardiac By-Pass and Elective Arrest with Autogenous Oxygenation

James A. Helmsworth, William R. Cole, James Neely and Ralph Shabetai, University of Cincinnati College of Medicine, Cincinnati, Ohio

Anomalies of the Aortic Arch — Development of the Aortic Arch

George H. Humphreys II, Columbia-Presbyterian Medical Center, New York, N. Y.

Left Heart Catheterization

G. H. Lawrence, Mason Clinic, Seattle, Washington

The Anatomical Correction of the Tetralogy of Fallot Defects Under Direct Vision, Utilizing the Pump-Oxygenator

C. Walter Lillehei, Richard A. DeWall, Herbert E. Warden, and Richard L. Varco, University of Minnesota Medical School, Minneapolis, Minnesota

A Syndrome of Congenital Defects Involving the Abdominal Wall, Diaphragm, Sternum, Heart and Pericardium

Mark M. Ravitch, Baltimore City Hospitals, Baltimore, Maryland

Mitral Commissurotomy

John V. Thompson and E. R. Eaton, Methodist Hospital, Indianapolis, Indiana

Excision of Epiphrenic Diverticulum of the Esophagus

Hawley H. Seiler, St. Joseph's Hospital, Tampa, Florida

ANNUAL CONVENTION, STUDENT AMERICAN MEDICAL ASSOCIATION

The 7th Annual Convention of the Student American Medical Association will be held at the Morrison Hotel, Chicago, May 1-4. More than a score of prominent physicians have accepted invitations to participate in the first full-scale scientific sessions, to be presented with the cooperation of the American College of Chest Physicians, the American College of Obstetricians and Gynecologists, and the William S. Merrell Company.

Dr. Theodore H. Noehren, Buffalo, New York, representing the Council on Undergraduate Medical Education of the American College of Chest Physicians, has arranged the following program to be presented Friday morning, May 2:

Presiding: Burgess L. Gordon, Albuquerque, New Mexico, President, American College of Chest Physicians

"The Incidence of Pulmonary Tumors in Mice Exposed to Aerosols of Therapeutic Agents"
James T. Post, Portland, Oregon (winner, 1957 College Essay Contest)

Discussion: David B. Radner, Chicago, Illinois

"Heart Surgery Today—Its Accomplishments and Promises"
Charles P. Bailey, Philadelphia, Pennsylvania

"Everything in the Book" (Discussion of 100 Cases of Chest Pathology) Theodore H. Noehren, Buffalo, New York

Discussion: Karl H. Pfuetze, Chicago, Illinois

X-ray Conference

Moderator: Herman J. Moersch, Rochester, Minnesota

Panel: J. Maxwell Chamberlain, New York City; John R. McDonald, Rochester, Minnesota; Colonel James A. Wier, Denver, Colorado

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College Chapter News

OKLAHOMA CHAPTER

A Pembine-type conference will be presented at the annual meeting of the Oklahoma Chapter, to be held jointly with the state Trudeau Society at the Western Hills Lodge, Waggoner, April 19-20. The program is as follows:

Saturday, April 19—Moderator: Richard M. Burke, Tulsa, President.

2:00 p.m. Introductory remarks: J. Floyd Moorman, Oklahoma City, President, Oklahoma Trudeau Society

"Ten Consecutive Admissions with Pulmonary Histoplasmosis, Missouri State Sanatorium, Mount Vernon"

"Evaluation of Pulmonary Function Studies"
Medical interpretation—William W. Stead, Gainesville, Florida
Surgical interpretation—Harry E. Walkup, Oteen, N. C.

6:00 p.m. Social hour

7:00 p.m. Dinner—James F. Hammarsten, Oklahoma City, presiding
Guest speaker: Harry E. Walkup

Sunday, April 20—Moderator: Allen E. Greer, Oklahoma City

9:00 a.m. "Ten Cases with Silico-tuberculosis Seen Prior to December, 1957, Eastern Oklahoma Tuberculosis Sanatorium"
Forrest P. Baker, Talihina

"Ten Consecutive Pulmonary Resections with Postoperative Space Problems"
Harley C. Darnall, State Sanatorium, Arkansas

12:15 p.m. Luncheon

Afternoon session—J. Lewis Yates, Mt. Vernon, Missouri

1:30 p.m. "A Group of Discharges with Collagen Vascular Disorders, Western Oklahoma Tuberculosis Sanatorium"
Glen P. Dewberry, Clinton

Critique
William W. Stead, Harry E. Walkup

4:00 p.m. Business meeting

MISSOURI CHAPTER

A joint meeting of the Missouri Chapter of the College and the Missouri Trudeau Society will be held at the Hotel Statler, St. Louis, Sunday, April 13. The program is as follows:

11:30 a.m. Business meetings

12:00 noon Luncheon

1:00 p.m. "Benign Obstructing Lesions of the Esophagus"
Duane Carr, Memphis, Tennessee
"Cineangiocardiography Method and Demonstration"
J. Girard Mudd, St. Louis
"Progress Report on Combined Therapy of Tuberculosis Using Pyrazinamide"
Bernard Friedman and Mario Pianetto, St. Louis

NEW JERSEY CHAPTER

The New Jersey Chapter will meet in Atlantic City, May 21, in conjunction with the annual meeting of the state medical society. The following program will be presented:

10:00 a.m. "Endoscopic Therapy of Lung Abscess"
A. Albert Carabelli, Trenton
"Fluoroscopic Determination of Pulmonary Stenosis—A New Sign"
Henry Green, Newark
"Familial Pulmonic Stenosis and Deaf Mutism—Clinical and Genetic Considerations"
Sanford M. Lewis, Lawrence Gilbert, David Biber, and Benjamin B. Sonnenblick, Ph.D., Newark
"Evaluation of Pleural Biopsy"
William B. Abrams, Maurice J. Small, East Orange
"Use of Meticorten in Chronic Pulmonary Tuberculosis"
Paul K. Bornstein, Asbury Park; Israel G. Epstein, G. Nair, Brooklyn, New York

12:30 Luncheon and business meeting

NEW ENGLAND STATES CHAPTER

The next monthly meeting of the New England States Chapter will be held at St. Vincent's Hospital, Worcester, Massachusetts, April 19. The following program will be presented:

9:00 a.m. Chairman: Heinz J. Lorge, Worcester, Massachusetts

Joint session with surgical section of St. Vincent's Hospital. Presentation of thoracic problems by Drs. Paul Ware, Oscar Ware and Oscar Feinsilver, Worcester:

"Pulmonary Sarcoidosis Associated with Bullous, Obstructive Emphysema" and "Cardiac Decompensation due to Co-existing Mitral Stenosis with Obliterative Pleuritis"

Symposium on Tuberculosis:

"The Present Status of Chemotherapy"
Paul Dufault, Rutland, Massachusetts
"The Changing Aspects of the Pathology of Pulmonary Tuberculosis"
Oscar Auerbach, East Orange, New Jersey
"Evaluation of the Available Techniques for Estimating the Virulence of the Tubercle Bacillus"
William Steenken, Jr., Saranac Lake, New York
"Ambulatory Treatment of Pulmonary Tuberculosis"
Emil Rothstein, Brockton, Massachusetts
"Pulmonary Embolism, Roentgenological Manifestations"
Felix G. Fleischner, Boston

12:50 p.m. Luncheon

2:00 p.m. Chairman: Rudolph Kurzmann, Cambridge, Massachusetts
"Principles of the Ventilatory Response in Pulmonary Emphysema"
Alvan L. Barach, New York City
Discussion: Maurice S. Segal, Boston
"Circulatory Diseases of the Lungs"
Robert P. McCombs, Boston
"Management of Diagnostic Problems Associated with Cancer of Lung"
Max G. Carter, New Haven, Connecticut
"The Present Status of Management of Carcinoma of the Esophagus"
John W. Strieder, Boston
"Results of Megavoltage Therapy of Esophageal Carcinoma and Cancer of the Lung"
Wayne P. Whitcomb, New Haven, Connecticut
Discussion: Richard H. Overholt, Boston

6:00 p.m. Dinner—Stockholm Restaurant. Welcome by Maurice S. Segal, Boston, chapter President.
Guest speaker: Dr. Hudson Hoagland, Executive Director, Worcester Foundation for Experimental Biology—"Basic Research in the Field of Cancer at the Worcester Foundation for Experimental Biology"

A tour of the city, including the Worcester Art Museum and Old Sturbridge Village, is being planned for the ladies. For advance dinner reservations ($6.00 each), please contact Dr. Oscar Feinsilver, 390 Main Street, Worcester 8, Massachusetts.

OHIO CHAPTER

The annual meeting of the Ohio Chapter will be held at the Netherland-Hilton Hotel, Cincinnati, April 16, in conjunction with the state medical association meeting. After luncheon at 12:00 noon, the following program will be presented:

"Experience in the Management of Spontaneous Pneumothorax"
Harvey Mendelsohn, Cleveland
"The Tuberculous Patient Two Years after Discharge from the Hospital"
Harold Humphrey, Columbus
"Surgical Treatment of Stenotic and Insufficient Lesions of the Aortic Valve"
Elmer Maurer, Cincinnati
"Trends in Tuberculosis as Demonstrated by Recent Hospital Admissions"
Herman Nimitz, Cincinnati

WISCONSIN CHAPTER

The Wisconsin Chapter will hold its annual meeting at the Schroeder Hotel, Milwaukee, Monday, May 5. The following program will be presented:

2:00 p.m. "Disseminated Indeterminate Pulmonary Lesions"
John R. McDonald, Rochester, Minnesota
"Significance of Heart Sounds in Clinical Medicine"
Aldo A. Luisada, Chicago, Illinois
"Physiologic Effects of Exercise in Pulmonary Emphysema"
Edwin R. Levine, Chicago, Illinois
"An Analysis of the Radiation Hazards and Rewards of Chest X-rays"
Jerome L. Marks, Milwaukee
"Physiologic Defects in Pulmonary Diseases"
George R. Meneely, Nashville, Tennessee
Panel discussion of subjects presented, with questions from the floor.

ARIZONA CHAPTER

The annual meeting of the Arizona Chapter will be held in Chandler, Thursday, May 1. Following a luncheon at 12:15, Dr. D. W. Melick, Phoenix, President, will preside over the business meeting. Dr. William B. Steen, Tucson, President-Elect, will preside over the following scientific program:

"Steroids in the Treatment of Patients Suffering from Pulmonary Tuberculosis"
Leo V. DiCara, Tucson

"Fungizone and Coccidioidomycosis"
Hans F. Stein, Tucson

"Report of VA-Armed Forces 17th Conference on Chemotherapy of Tuberculosis"
Solomon Netzer, Tucson

"Graphic Diagnosis of Pulmonary Heart Disease"
Hyman Fisher, Tucson

"The Middle Lobe Syndrome"
Leon L. Titche, Tucson

FLORIDA CHAPTER

The annual meeting of the Florida Chapter will be held at the Americana Hotel, Miami Beach, Sunday, May 11. The following program will be presented:

8:45 a.m. Business meeting

9:10 a.m. "Association of Chronic Obstructive Pulmonary Emphysema with Chronic Peptic Ulceration"
Louis Zasly, Delray Beach

"A Comparison of Clinical with X-ray and Pulmonary Function Laboratory Estimation, Timed and Total Vital Capacity"
Milton B. Cole, Bay Pines

"Dysphagia"
Myron I. Segal, Hollywood

"Clinical Significance of Solitary Pulmonary Nodules: 60 Collected Cases with Roentgenologic and Pathologic Correlations"
Franklin G. Norris, Orlando

"Anticoagulants in Impending Myocardial Infarction"
E. Sterling Nichol, Miami

"The Use of Prednisolone in Far Advanced Pulmonary Tuberculosis: Report of Four Seriously Ill Colored Females Who Had Failed to Respond to Conventional Therapy"
Mary Lou McIlhany, Lantana

"Management of Carcinoma of the Lung in Elderly and Poor Risk Patients"
DeWitt C. Daughtry, Miami

12:00 noon Luncheon

1:00 p.m. "Fungus Diseases of the Lungs"
David T. Smith, Durham, North Carolina

"Surgical Aspects of Diaphragmatic Hernia"
James Moody, Orlando

X-ray Conference (physicians are requested to bring x-rays for discussion after presenting a brief clinical history)

NEWS NOTES

Dr. Arthur M. Olsen, Rochester, Minnesota, visiting physician pro tem of the Lovelace Foundation, Albuquerque, New Mexico, spoke on "Pulmonary Complications of Esophageal Disease" and "Esophageal Motility Studies" during a two-day scientific session in Albuquerque March 6 and 7. In addition, Dr. Olsen participated in several panel discussions dealing with pulmonary and esophageal disease.

Dr. J. L. Ehrenhaft, Iowa City, Iowa, recently spoke at a scientific seminar sponsored by the Northwest Iowa Heart Council, the Clay County and Northwest Iowa Medical Societies in Spencer.

ADVANCE REGISTRATION

.....Member .....Non-member

There is no registration fee for members.
The registration fee for non-members is $25.00.

Please Print

Name .....

Address .....

City and State.....

Accompanied by .....

Hotel .....

Arrival .....Departure .....

Remarks .....

.....

.....

.....

I am enclosing my check in the amount of $.....for reservations as indicated on the reverse side of this form.

Return this form to: American College of Chest Physicians
112 East Chestnut Street
Chicago 11, Illinois

URGENT NOTICE

By completing this form and returning it at once to the Executive Offices of the College, you will avoid having to stand in line at the Registration Desk in San Francisco. Your badge and program, as well as luncheon, banquet and seminar tickets, will be prepared in advance and will be awaiting your arrival at the Fairmont Hotel. Please complete both sides of this Advance Registration Form and mail promptly. Thank you.

Non-members must enclose a registration fee of $25.00 with this form.

Please make checks payable to **American College of Chest Physicians**

RESERVATION FORM

Seminars, Wednesday, June 18

Members: $7.50 each session
Non-members: Included in $25.00 registration fee

Morning Sessions (9 a.m.-12 noon)

First choice A.M.....

Second choice A.M.....

Afternoon Sessions (2:00-5:00 p.m.)

First choice P.M.....

Second choice P.M.....

Please indicate choice by number as listed in program

Round Table Luncheons **$4.00 each**

	Friday, June 20	Saturday, June 21	Sunday, June 22
First choice	A-.....	B-.....	C-.....
Second choice	A-.....	B-.....	C-.....
Third choice	A-.....	B-.....	C-.....

Please indicate choice by number as listed in program

PRESIDENTS' BANQUET

Saturday, June 21, Fairmont Hotel, San Francisco

Cocktails—Dinner—Dancing ***Tickets: $7.50 each***

All places at the Annual Presidents' Banquet are reserved. Tables will be assigned in order of requests received. Please order your tickets at once so you may be assigned your table early. Tables for ten may be reserved upon receipt of payment for tickets and names of persons in the party. This is the gala College evening of the year and you will not want to miss it!

I wish to reserve.....tickets for the Annual Presidents' Banquet Saturday, June 21, 7:00 p.m. (price includes cocktails, dinner and dancing).

Please complete coupon on reverse side

NOTE: Make checks payable to **American College of Chest Physicians.** Checks must accompany all requests for reservations and will be accepted in the order received. All tickets will be held for pick-up at the College Registration Desk, Fairmont Hotel, San Francisco.

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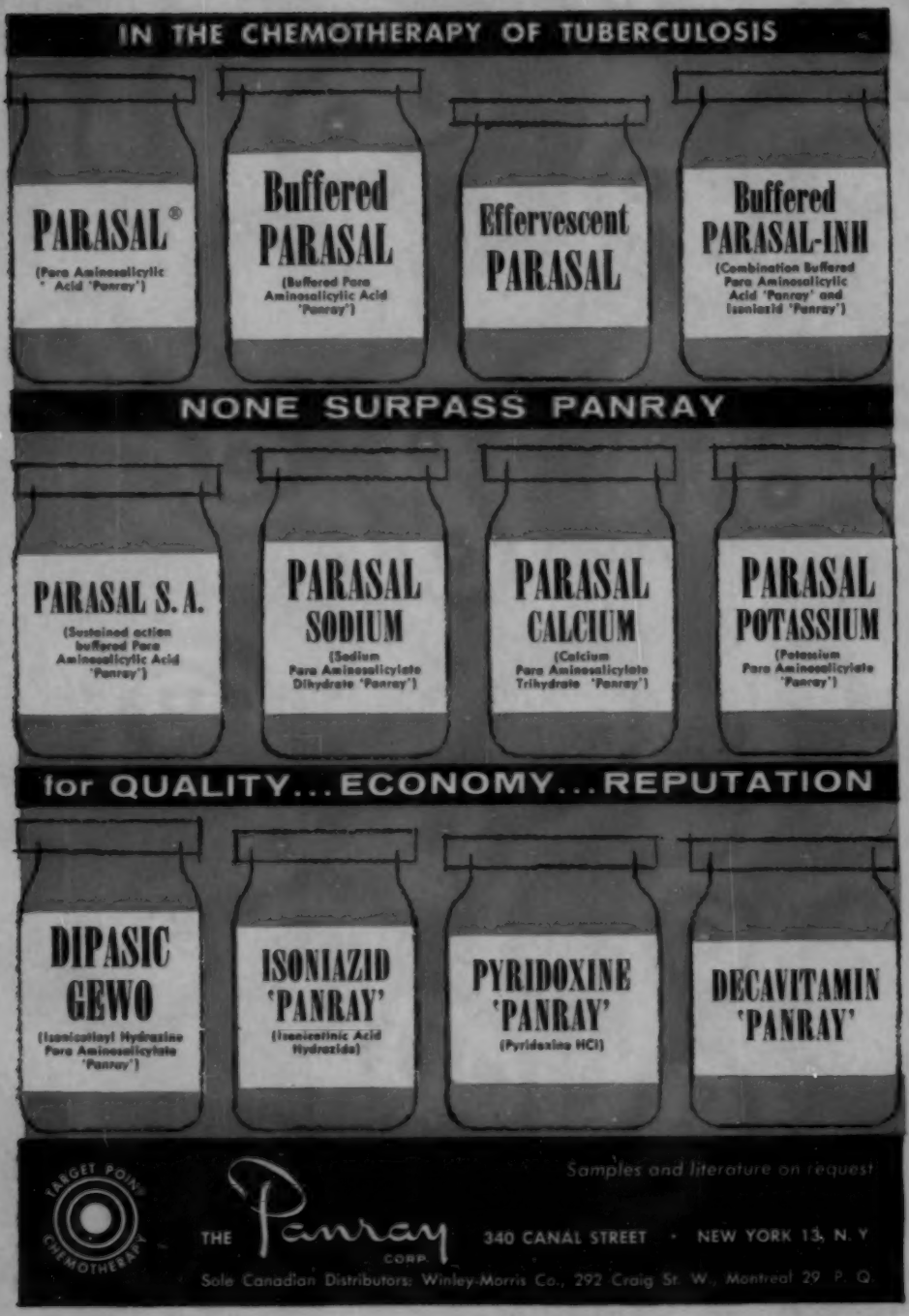
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